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MEDICAL NEWS LETTER

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Policy

The U.S. Navy Medical News Letter is basically an official Medical Department publication inviting the attention of officers of the Medical Department of the Regular Navy and Naval Reserve to timely up-to-date items of official and professional interest relative to medicine, dentistry, and allied sciences. The amount of information used is only that necessary to inform adequately officers of the Medical Department of the existence and source of such information. The items used are neither intended to be, nor are they, susceptible to use by any officer as a substitute for any item or article, in its original form. All readers of the News Letter are urged to obtain the original of those items of particular interest to the individual.

Change of Address

Please forward changes of address for the News Letter to Editor: Bureau of Medicine and Surgery, Navy Department, Washington, D.C. 20390 (Code 18), giving full name, rank, corps, and old and new addresses.

FRONT COVER: U.S. NAVAL HOSPITAL, YOKOSUKA, JAPAN. The U.S. Naval Hospital, Yokosuka, Japan is located within the confines of the U.S. Naval Fleet Activities, in the city of Yokosuka, Japan which has a population of 308,314 people and is located on the Miura Peninsula, approximately forty miles south of Tokyo. Construction by the Japanese Navy of what is now the U.S. Naval Hospital, Yokosuka, was commenced on 31 March 1927 and completed on 20 February 1931. During World War II this hospital was occupied as an Imperial Japanese Navy Medical Center which included a Hospital Corps Training School and a Naval Hospital which had a normal staff of 237 and a war-time staff of 735 officers and men. The bed capacity was listed then as 578 normal, 690 maximum, and 857 emergency. The buildings in the present U.S. Naval Hospital compound are substantially the same as when it was originally constructed by the Japanese Navy.

Shortly after the start of the Korean Conflict the U. S. Naval Hospital was established by the Secretary of the Navy and it was commissioned on 11 September 1950. The month of December 1950 brought the hospital's greatest work load, the peak in patient census being reached on 14 December 1950 when there were 4,388 on the sick list. Once during this period there were 2,000 patients admitted within a 24 hour time span.

In December 1951 the Secretary of the Navy awarded the Navy Unit Citation to the U.S. Naval Hospital, Yokosuka, "For extremely meritorious services in the treatment and hospitalization of 5,804 war casualties and other patients from 5 December 1950 to 15 January 1951." CAPT Walter F. James MC USN (later RADM rank) was the hospital's Commanding Officer at the time of the record patient load.

The issuance of this publication approved by the Secretary of the Navy on 4 May 1964.

Surgeon General Receives Third Star

The Surgeon General of the Navy, Robert B. Brown, was promoted to the rank of vice admiral on October 27, 1965. Legislation for three-star rank for the Surgeons General of the Army, Navy, and Air Force was sponsored by Congressman L. Mendel Rivers, Chairman of the House Armed Services Committee.

Admiral Brown, obviously proud, remarked "This promotion is truly a recognition of the contributions of all of you in the Navy Medical Department, past and present, Reserve and Regular. I can only say that I am very happy to have been an incumbent of the office when this action was completed."

TREATMENT OF PULMONARY EMBOLIC DISEASE*

A Critical Review of Some Aspects of Current Therapy

*Duncan P. Thomas MD, PhD**, Boston, Mass.* *The New Eng J Med 273(17): 885–892, October 21, 1965.*

The evidence continues to accumulate that pulmonary embolic disease represents a major cause of death, especially among patients in hospitals. Smith, Dexter and Dammin, in autopsy studies at the Peter Bent Brigham Hospital, Boston, found pulmonary embolism to be the single most common cause of death. Freiman found evidence of old or recent pulmonary emboli in 64 per cent of a group of consecutive patients autopsied at the Beth Israel Hospital, Boston. Morrell, Truelove and Barr, impressed by an apparent fivefold increase in the number of patients given the diagnosis of pulmonary emboli at the United Oxford Hospitals in the past decade, concluded that this increase represented "one aspect of an epidemic of thrombotic disease at present affecting Western society." Although the importance of this disease is now generally recognized, and significant advances have been made in the areas of pathogenesis and diagnosis, the therapy of pulmonary embolic disease remains controversial. In fact, the therapeutic guidance that has been offered has been characterized as follows: ". . . some of it has been without experimental basis, some has been lacking in clinical sense, and the bulk has been woefully deficient in both."

In this review, some of the therapeutic measures currently employed in the prophylaxis and treatment of pulmonary embolic disease will be examined in the light of current knowledge of the pathophysiology of the disease. The evidence for their effectiveness will be evaluated on the basis of present-day standards for clinical trials. Some recent work on experimental thromboembolism will be reviewed, although much will be omitted for the sake of brevity.

Medical Management

Experimental Background

It has become clear in recent years that thrombosis occurring in areas of stasis or low-velocity blood flow, such as veins, represents a somewhat different phenomenon from that occurring in areas of high-velocity blood flow. In the former type, the thrombus is more akin to a blood clot and is termed a red, or coagulation, thrombus. Arterial thrombi, on the other hand, have a different structure, and the fundamental event appears to be an initiating platelet nidus. Wessler, in stressing the difference between venous and arterial thrombi, has suggested that the two primary pathogenetic events in the formation of venous thrombi are local stasis, such as occurs in the leg veins, simultaneously combined with systemic altered coagulability of the blood. According to this view of the pathogenesis of venous thrombi, therapeutic attempts should revolve around reducing venous stasis in the legs and countering the assumed systemic hypercoagulability. A detailed regimen of medical management based on these concepts has been outlined.

It has been shown experimentally that venous thrombi neither form nor propagate in animals given sufficient heparin to prolong the glass clotting time to greater than twice the control value. Recent observations in dogs have indicated that heparin may have an additional function in the treatment of pulmonary emboli, apart from preventing thrombus formation or propagation. After the release of autologous venous thrombi to the lungs of dogs, intense airway constriction developed within one or two minutes, owing to the release of serotonin from platelets. However, if the dog was heparinized before the release of thrombi to the lungs, airway constriction did not develop. Heparin prevented the release of serotonin from platelets, probably by neutralizing thrombin still present on fresh thromboemboli. According to this concept, thromboemboli obstructing segments of the pulmonary vasculature may have profound pharmacologic as well as mechanical effects by inducing the local release of platelet amines, resulting in airway constriction and vasoconstriction. The extent to which rapid smooth-muscle constriction in the airway and pulmonary vasculature contributes to the sudden death seen in

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pulmonary embolism remains conjectural. It is not without interest, however, that there are clinical reports indicating that fatal pulmonary embolism is very uncommon once a large dose of heparin has been administered intravenously. Bronchoconstriction observed in patients with acute pulmonary embolism was found to be partially reversed after heparin therapy, suggesting that thrombin-induced platelet amine release may occur in man.

Prophylactic Therapy of Venous Thromboembolism

The rationale for selected prophylactic therapy is based primarily on two well recognized clinical facts —namely, that certain patients are notoriously liable to have pulmonary emboli and that the diagnosis of venous thromboembolism is very difficult. It follows, therefore, that in certain high-risk groups, prophylactic therapy may be warranted. The classic paper of Sevitt and Gallagher demonstrated convincingly in a well controlled study that prophylactic anticoagulant therapy could virtually abolish thromboembolic complications in elderly patients with fracture of the neck of the femur. As Sevitt recognized, it is necessary to strike a balance between the indiscriminate administration of anticoagulant therapy to every patient admitted to the hospital and its too narrow restriction. He found in injured patients that the great majority of cases of embolism occur in patients over forty-five years of age and that deep vein thrombosis is especially likely to occur in patients over this age who are put to bed for more than three days.

Sevitt's current policy is to institute oral prophylaxis from the day of admission in all patients over the age of forty years with a fractured neck of the femur, other fractures of the femur, fractured tibia and fractured ankle. In his experience, hip pinning and nailing and other limb surgery can be carried out under phenindione therapy without the added danger of operative bleeding. Therapy is continued for one week beyond the time when the patient is ambulant. Salzman and his associates, at the Massachusetts General Hospital, have recently confirmed Sevitt's observations. They studied 187 patients with fracture of the neck of the femur, dividing them equally into control and treated groups. In their control group, 8 patients had pulmonary emboli, with 4 deaths. None of the patients on anticoagulant therapy suffered a pulmonary embolus. Dick et al., in another well controlled study, demonstrated the effectiveness of prophylactic anticoagulant therapy for venous thromboembolism. Bottomley, Lloyd and Chalmers, after ten years' experience with prophylactic anticoagulant therapy in postoperative gynecologic patients, considered the frequency of thrombotic disease to be reduced by a factor of five, although they did not have a concurrent control group of matched patients. It seems clear, therefore, that provided the drug is given early, for sufficient time and under proper laboratory control, thromboemboli can be prevented by prophylactic anticoagulant therapy.

Provided careful screening of patients is carried out, excluding those with accepted contraindications to anticoagulant therapy, serious hemorrhagic complications are few. Sevitt and Gallagher had 2 major complications in their control group, and 5 in the phenindione-treated group, with no deaths. Bottomley et al. reported a total incidence of bleeding of 4.2 per cent but only 0.8 per cent of patients required either transfusion or further medical treatment; in prophylactic therapy in 3,777 postoperative gynecologic patients, only 1 death was attributed to anticoagulant therapy. The apparent reluctance of many physicians to employ prophylactic anticoagulant therapy, even in high-risk patients, is probably due to excessive fears about hemorrhagic complications and insufficient recognition of the effectiveness of anticoagulant therapy in venous thrombosis. As recently suggested, there is a potent but subtle explanation for this reluctance to employ a prophylactic therapy; it is not easy to employ a mode of therapy in which success cannot be recognized in the individual patient but in which a deleterious hemorrhagic complication of therapy is readily apparent.

Therapy of Overt Pulmonary Embolism

Heparin has been used in the treatment of venous thrombosis for nearly thirty years, and reports that such therapy reduced the number of deaths from pulmonary embolism go back to the late 1930's. Reporting on the early Swedish experience, Jorpes wrote that the results after anticoagulant therapy in venous thromboembolism were "as striking as any hitherto reported following the introduction of a specific therapy in medicine." Bauer has recently reviewed his experience with heparin therapy for venous thrombosis. Of 59 patients with pulmonary emboli complicating venous thrombi, and treated with heparin, 2 died from complicating bronchopneumonia whereas the remaining 57 patients survived. Many of these patients were in poor condition because of massive embolism, and 10 had had repeated attacks. However, it was not until 1960 that Barritt and Jordan reported a study in which a concurrent series was observed, assigning patients by ran-

dom selection into treated and control groups. A total of 35 patients in whom the diagnosis of pulmonary embolism was made, and in whom there was no contraindication to anticoagulant therapy, were admitted to the study. Of the 19 untreated cases 5 died, and 5 others had nonfatal recurrences of embolism. The 1 death in the treated group was due to a combination of suppurative pneumonia and gastrointestinal bleeding. At this point in the trial no further patients were admitted to the untreated group, but 38 others were taken into the treated group, making a total of 54. There was only 1 further death, which was due to renal tubular necrosis from an adverse effect of the anticoagulant, phenindione. The form of therapy employed was 10,000 units of heparin given intravenously every six hours for six doses, with concurrent oral administration of a coumarin derivative (Nicoumalone), which was continued for fourteen days. In these 2 series the mortality rate in patients with pulmonary embolism placed on anticoagulant therapy was about 4 per cent, although in both series the deaths were apparently not due to pulmonary emboli. In other studies the incidence of fatal pulmonary emboli after anticoagulant therapy ranged from 0 to 2.2 per cent. In contrast, the mortality rates in 2 series in which the patients received no specific treatment were 26 per cent and 32 per cent, respectively.

The optimum dose of heparin that should be given to a patient with an acute pulmonary embolus is unsettled. The minimum dose appears to be one that keeps the clotting time in excess of twice the control value at all times, for venous thrombi will not form or propagate experimentally under such conditions. However, the dose of heparin required to prolong the clotting time varies considerably, especially in the patients who have an acute thrombus. It is not without interest that the workers who have claimed the greatest success with heparin therapy have usually given at least 40,000 units of heparin per day during the initial therapy. Whether adequate heparin therapy for an acute embolus can also be given by the subcutaneous or the intramuscular route is as yet uncertain. There is some evidence that subcutaneous and intramuscular heparin therapy may occasionally be complicated by arterial emboli.

Pulmonary embolic disease due to recurrent showers of small emboli tends to have an insidious onset and leads to obliterative pulmonary hypertension, owing to the gradual destruction of the pulmonary vascular bed by microscopic thromboemboli. These patients are often post-partum women, in whom the only presenting symptoms may be dyspnea, fatigue and early signs of strain of the right side of the heart. In such cases, if the diagnosis is not made early, and anticoagulant therapy is not given promptly, the pulmonary hypertension becomes irreversible, and death from intractable failure of the right side of the heart results in a period of months to years. A few cases have been reported in which this sequence appears to have been prevented by anticoagulant therapy. In 1 patient with established thromboembolic pulmonary hypertension, a marked fall in pulmonary-artery pressure followed eighteen months of anticoagulant therapy; five months after the cessation of therapy the signs of pulmonary hypertension reappeared. These signs again disappeared when the anticoagulant therapy was reinstituted. Despite encouraging case reports such as this one, the overall prognosis in patients with established obliterative pulmonary hypertension is poor, and in the series reported by Goodwin et al., 11 out of 19 patients died over a five-year period. However, as Goodwin pointed out, the failure of anticoagulant therapy in this group was probably due to late diagnosis and treatment.

Fibrinolytic Therapy

Reports on the use of fibrinolytic agents in pulmonary embolism are beginning to appear. Israel et al. found that anticoagulant therapy combined with fibrinolytic therapy gave results that were superior to anticoagulant therapy alone. However, the study compared results on one service (anticoagulants) with results on another service (anticoagulants and fibrinolysin), which is a technic that does not allow separation of the effects of therapy from those of selection. For example, they found a 40 per cent mortality in the patients who were given anticoagulant therapy alone, which is considerably in excess of that reported in most series. In 4 of their patients treated with fibrinolysin serum hepatitis subsequently developed. They concluded that treatment of pulmonary embolism by fibrinolysin was advisable only if the hazard of serum hepatitis could be eliminated.

Sautter et al. have reported 2 cases of complete resolution of massive pulmonary thromboembolism, documented by arteriography. In neither was thrombolytic therapy employed, and in 1 of the patients complete radiologic resolution occurred in twenty-five days. Fred and his co-workers have recently reported that in 4 patients with pulmonary emboli, but without pre-existing cardiorespiratory disease,

repeat pulmonary angiograms nine to nineteen days later showed complete disappearance of the obstructive lesions. No thrombolytic therapy was employed. These important observations represent a clinical confirmation of what has already been shown in dogs, in which autologous venous thromboemboli were found to be rapidly lysed. Although future developments in this field will be observed with great interest it is likely that the therapeutic role of fibrinolytic drugs in thromboembolism will not be easy to evaluate. It is apparent that the body possesses potent fibrinolytic mechanisms, and to assess the contribution of exogenous fibrinolytic drugs in the treatment of thromboembolic disorders will require careful prospective studies, with proper randomization of patients into control and treated groups.

Surgical Management

Over the years, the development of surgery for thromboembolic disease has ranged from superficial femoral ligation to common femoral ligation, thence to vena-cava ligation and finally to pulmonary embolectomy. The basic premise of venous ligation is that the great majority of emboli originate from the lower limbs and that by interruption of the main venous channels to the heart, the blood is forced to travel via smaller collateral channels. Large emboli are therefore prevented from traveling to the lungs from the legs, and death from massive pulmonary embolism is averted. It is apparent that there is a compelling simplicity to the surgical rationale for venous ligation. Similarly, if the pulmonary-outflow tract is occluded by a massive embolus, its prompt removal would obviously benefit the circulation. It will be argued, however, that the problem is not as clear cut as it appears.

Venous Ligation

The value of venous ligation in thromboembolism either prophylactically or therapeutically, is difficult to determine from the literature, largely because the studies reported have been retrospective, with no randomization of patients. The errors inherent in such types of study are well recognized, and the wide variations in reported results are probably due largely to biased sampling. For example, at 4 different hospitals in the same city, the mortality from pulmonary embolism after femoral-vein ligation has been reported as varying between 0.6 per cent and 7.0 per cent. In the same series, the mortality in the patients who were treated with anticoagulant therapy varied from 2.1 per cent to 24 per cent. The difficulty in evaluating such results is compounded by the fact that in many patients who receive anticoagulant therapy venous ligation is also performed.

If clear distinctions are not drawn between the types of operation (such as superficial or common femoral ligation) and the type of anticoagulant therapy employed (such as heparin or a coumarin derivative) it becomes impossible to make valid comparisons. Properly controlled clinical trials, with separation of patients into clearly defined treatment groups, and assignment of patients by random selection, are essential before modes of therapy can be compared. Although it would obviously be unethical to withhold therapy from a patient with established pulmonary embolic disease, a prospective study of, for example, the comparative mortality and morbidity after vena-cava ligation and heparin therapy would be justified.

The present emphasis in the surgical literature appears to be on the superiority of vena-cava over femoral-vein ligation. This area has recently been well reviewed by Crane on the basis of his large experience. In the absence of heart disease he found the in-hospital mortality to be 5 per cent with the latter and 2 per cent with the former. The incidence of postoperative morbidity was almost twice as high after femoral-vein ligation as after vena-cava ligation. However, in patients with heart disease the in-hospital mortality with either type of ligation varied from about 20 per cent in patients with failure of the left side of the heart to 40 to 50 per cent in those with right-sided failure. Crane concluded that vena-cava ligation had not been demonstrated to increase the patient salvage in late-stage congestive heart failure. Krause et al., reviewing their experience in 55 cases of vena-cava ligation, claim that the operation had been 100 per cent effective in preventing recurrent pulmonary embolism. They had 3 operative deaths and 7 late deaths due to other diseases. However, 30 of their patients still living had been followed for less than two years. Mozes and his associates, in a study of 74 patients who had vena-cava ligation, reported 4 operative deaths and a further 4 deaths from pulmonary emboli after ligation, giving a total failure rate of 11 per cent due to immediate mortality. These 3 papers, representing some of the recent larger series, suggest that vena-cava ligation can be performed with an operative mortality of approximately 2 to 5 per cent in patients without heart failure. The late mortality ranges from a further 5 per cent to 50 per cent, depending on the cardiac status of the patient.

The reported morbidity after vena-cava ligation has varied greatly from series to series. In a large

series presented by Ochsner 45 out of 117 patients had no sequelae, 13 patients had mild edema, 28 had edema controlled by bandaging, and 5 had edema controlled by bandaging and periodic elevation of extremities. No patients had incapacitating sequelae. Similarly, Krause et al. described the morbidity as being "minimal." However, Mozes and his co-workers found severe sequelae in 12.5 per cent of patients, and Crane reported that 10 per cent of his patients had marked acute leg edema. Donaldson and his associates, on the other hand, reported that 50 per cent of their patients had incapacitating late sequelae. Several surgeons have stated their belief that post-operative swelling results from pre-existing venous thrombosis, and not from the ligation of a major vein. This may well explain some of the wide variations in the reported incidence of sequelae.

In an attempt to minimize the edema associated with complete interruption of the vena cava, modifications have been introduced in which the lumen of the vessel is narrowed sufficiently to prevent the passage of massive emboli, but not to prevent the flow of blood. Teflon clips and interrupted mattress sutures (plication) have been the two main technics employed. Spencer et al. described 39 patients who had plication of the vena cava, with no pulmonary emboli within the first few months after operation. They commented that plication should not be done in patients with pulmonary hypertension from repeated small emboli, because such emboli could pass through the 3-mm channels constructed with plication. De Weese and Hunter reported their result in 24 patients in whom they placed a filter in the inferior vena cava. Seven of them died over a five-year period, although none apparently died from thromboembolism. However, the recognition of small pulmonary emboli at postmortem examination is difficult unless special technics are used, and these patients would be unlikely to die from large emboli, owing to the protective effect of the filter. Bergan et al. reported that of 10 patients on whom cavography was performed after plication, the vena cava was in fact occluded in 6. In their series vena-cava plication appeared to have no significant advantage over ligation. They made the important point that the clinical evaluation of a patient can be deceptive. Seven out of their 10 patients were assumed to have a patent vena cava before cavagrams, but only 3 had a patent vessel demonstrated by cavography. Moretz has reported that of 10 patients in whom a follow-up study was performed, the vena cava was not patent in 4. It seems probable, therefore, that in a high proportion of patients, plication of the inferior vena cava is converted into complete occlusion by trapped emboli.

A study of the pathophysiology of pulmonary embolic disease leads one to question some of the rationale behind venous ligation as a mode of therapy, at least regarding its long-term effectiveness. It may be taken as axiomatic that after venous ligation, the blood returns to the heart via collateral veins. Over a length of time these collateral channels enlarge in response to the increased volume of blood that they carry. For example, films obtained several months after vena-cava ligation demonstrate numerous enlarged collateral channels large enough to allow small emboli to reach the lungs. Even clinically recognizable pulmonary emboli follow ligation of the inferior vena cava, and Gurewich and Thomas collected 8 such cases over a two-year period. In 2 of their patients the recurrence after caval ligation was documented by angiography, and in the others, the symptoms and signs, including characteristic radiologic and electrocardiographic changes, were highly suggestive of pulmonary emboli. Davis et al. recently suggested that recurrent embolization from a cul-de-sac formed by poor location of the vena-cava ligation may also be responsible for some of the apparent failures. They recommend that ligation be performed just below the renal veins and that the cava be divided to avoid a cul-de-sac, where thrombosis can occur, with subsequent embolization.

It is now well recognized that multiple small emboli can produce death from failure of the right side of the heart. Indeed, there is experimental evidence that acute cor pulmonale can be produced solely by platelet microemboli. If, as has been suggested, the spectrum of pulmonary embolic disease ranges from acute massive emboli through multiple small emboli to diffuse microemboli, it becomes apparent that only massive emboli are likely to be prevented by ligation. Of the total deaths from pulmonary emboli the percentage resulting from massive emboli is unknown. It seems likely, however, that more patients die from multiple small emboli than has been recognized in the past. In 34 patients whose deaths were attributed to pulmonary embolism, Smith et al. found multiple emboli in all cases. Post-mortem arteriography demonstrated approximately five times the number of emboli found by routine post-mortem examination, showing that small emboli can easily be missed on gross dissection of the lungs. Of particular interest was their observation that emboli were most commonly found in muscular arteries, approxi-

mately 85 per cent of which are less than 1 mm in internal diameter. Only 8 of the 34 patients had emboli in the large elastic arteries. Although many of these small emboli may have "seeded" from larger emboli trapped in the right ventricle the implication of this work seems to be that a primary factor in pulmonary embolic disease is the occurrence of multiple small emboli, which gradually occlude the pulmonary vascular bed. These emboli may reach the lungs by collateral channels even after the inferior vena cava has been tied.

Pulmonary Embolectomy

The operation of pulmonary embolectomy has recently been receiving increasing attention, and numerous case reports of successful embolectomies have appeared in the recent literature. Although successful results from the Trendelenburg operation are being reported the technic of pulmonary embolectomy with cardiopulmonary bypass is now considered the operation of choice. Donaldson and his associates believe that at least one-fifth of the patients dying from massive embolism survive long enough to allow institution of a planned operative procedure. The crux of the issue, however, is the decision when to operate. Hampson et al. suggest that the correct time is when the patient is failing to respond to conservative measures, and in their experience if the patient does not respond to oxygen, morphine and heparin within thirty minutes, recovery is unlikely. Hayward and Howqua, in reporting a successful Trendelenburg operation, stress the point that the embolectomy should be regarded as an incident during the course of medical treatment for pulmonary embolism, and not as an alternative to this treatment. They believe that, after embolectomy, the patient must be assumed to be still suffering from pulmonary embolism and still in need of the medical treatment for it. A recent editorial suggested that a new period of more active therapy for massive pulmonary embolism is arriving. If this is so, perhaps it is permissible to raise certain questions, while the matter is still *sub judice*. As Donaldson and his co-workers noted, the greatest challenge lies in the decision to proceed with operative intervention in critically ill patients, some of whom will recover spontaneously. The challenge is particularly great since there is evidence that intravenous administration of herapin represents a highly effective mode of therapy in the patients who do not die immediately from massive pulmonary embolism. The only way to resolve such a problem is for a large general hospital, or group of hospitals, to undertake a prospective controlled trial of therapy, comparing the effects of pulmonary embolectomy with heparin therapy. The example of a recent cooperative prospective study of the role of surgery (portacaval shunt) in portal hypertension could well be followed. Such a study is not as unrealistic as it might at first appear, for Sautter has already reported 5 personally performed embolectomies. Despite the obvious difficulties, a controlled trial is needed before opinions become crystallized solely on the basis of personal experience.

Acute Venous Thrombosis

The treatment of acute venous thrombosis ("acute phlebitis") has recently been reviewed and will not be considered in detail here. However, certain aspects of the therapy of pulmonary embolism apply, *pari passu,* to venous thrombosis. The major hazard to patients with peripheral venous thrombosis is pulmonary emboli, and it seems reasonable to conclude that patients in whom the diagnosis of venous thrombosis has been made should be considered candidates for prophylactic therapy. A patient with overt thrombophlebitis is clearly in a "high-risk" category in relation to the possibility of embolism. The proved efficacy of anticoagulant therapy in preventing embolic complications of venous thrombosis with minimal hazard of hemorrhage, indicates that this is the treatment of choice. If current concepts of the pathogenesis of venous thrombosis are correct it is also more physiologic to employ an agent that reduces systematic hypercoagulability without increasing local stasis. If this argument is followed further there seems to be little therapeutic rationale in separating superficial from deep venous thrombosis or thrombosis in the legs from thrombosis in the thighs. If it is borne in mind that the clinical diagnosis of venous thrombosis is highly inaccurate any overt evidence for thrombosis suggests that the patient may be in a thrombotic state, with a propensity for forming thrombi at other sites. Although a patient may appear to have an acute superficial thrombophlebitis in the calf the presence of a concomitant silent deep venous thrombus cannot be excluded by clinical examination. Hafner et al. found that in 17 per cent of patients with the diagnosis of superficial thrombophlebitis, at operation deep thrombophlebitis had in fact also developed. A further 2.3 per cent had evidence of pulmonary embolism. In this series of 133 patients, therefore, 1 in 5 of those who appeared to have only superficial

thrombophlebitis did in fact have a potentially lethal condition. It seems more logical to regard the presence of thrombosis in an acute form at any site as an indication of a thrombotic state, which should, ipso facto, be treated with prophylactic anticoagulant therapy. The treatment prevents propagation of a thrombus, but more important is the fact that it is also prophylactic therapy for pulmonary embolism.

Discussion

It is apparent that no universal agreement exists on the proper management of pulmonary embolic disease. Many of the data supporting the various modes of therapy do not stand up to critical examination. In particular, there are few data in which one mode of therapy has been concurrently compared with another, a proper comparison of relative effectiveness thus being made very difficult. Although recent experimental work has enlarged the understanding of the pathogenesis of venous thrombosis, the extent to which these findings are applicable to man is still unclear. However, as Samuel Butler pointed out, "Life is the art of drawing sufficient conclusions from insufficient premises," and the following general conclusions are offered in the belief that they represent a reasonable basis for treatment in the present state of knowledge.

Convincing evidence exists that prophylactic anticoagulant therapy should be employed in patients with illnesses in which there is a high incidence of thromboembolic complications. Patients with immobilizing fractures, burns, previous history of thromboembolism and congestive heart failure fall into this category. In a particular patient the point at which the hazards of thromboemboli exceed the hazards of therapy can only be decided on the basis of good clinical judgment. However, it seems likely that many physicians have tended to underestimate the former and overestimate the latter. The treatment of choice for an acute pulmonary embolus is intravenous heparin therapy. The length of time that heparin should be administered is unclear. Barritt and Jordan gave only 6 doses and followed this by an orally administered drug for two weeks. Bauer gave intravenous heparin until the patient was fully mobilized. Others have recommended that heparin therapy be continued for a minimum of eight to ten days, which is the time required for firm adherence to the vein wall of experimentally produced bland thromboembolism. It seems reasonable to conclude, therefore, that heparin should be given at least until oral therapy has adequately depressed the prothrombin time.

The indications for long-term anticoagulant therapy are not yet well established. Barker and Priestly reported a 30 per cent recurrence of pulmonary embolism in 381 patients who had had an initial pulmonary embolus and survived. In many cases it is clear that pulmonary embolism is a recurrent disease, and it seems logical, therefore, that such patients should be placed on anticoagulant therapy for an indefinite period. Patients who have thromboembolic obliterative pulmonary hypertension cannot afford to suffer further emboli, and should be placed on permanent anticoagulant therapy. However, in many patients the advisability of long-term therapy is more difficult to determine, for they have neither recurrent disease nor established pulmonary hypertension. Although it is clear that the minimal length of therapy is until the patient is fully mobile, the optimal length is uncertain. Nevertheless, there is a growing tendency to treat patients for six to twelve months, particularly if the emboli occur "spontaneously." This practice is based on the clinical impression that pulmonary emboli are particularly apt to recur within this period.

Venous ligation has a definite place in the therapy of pulmonary embolic disease, although the extent to which it should be employed is disputed. However, there is general agreement that in the patients in whom a contraindication to anticoagulant therapy exists, or in whom pulmonary emboli are occurring in the face of adequate anticoagulant therapy, vena-cava ligation is the treatment of choice. And yet patients in whom emboli continue to form despite adequate heparin therapy, and who then have inferior vena-cava ligation, should also be placed back on heparin therapy after operation. It is doubtful whether femoral-vein ligation alone, either superficial or common, gives adequate protection against either an initial or a recurrent pulmonary embolus. The patients who collapse with a massive pulmonary embolus, and who do not respond rapidly to conservative measures, including immediate intravenous infusion of heparin, are candidates for a pulmonary embolectomy if the facilities are readily available. However, the evidence suggests that the great majority of patients suffering from massive pulmonary embolism either will die before any therapy can be administered or will respond to prompt and vigorous medical therapy.

Finally, although the pathogenesis of pulmonary embolic disease has yet to be fully elucidated, and

although diagnosis still presents a great challenge, it is believed that the wider application of current knowledge, especially in the areas of prophylaxis, would do much to reduce the toll of the disease.—(The many references of this article can be seen in the original article in the New Eng J Med.)

THE DIAGNOSIS AND TREATMENT OF WHIPPLE'S DISEASE

Julian M. Ruffin MD and W. M. Roufail MD. Am J Digestive Diseases 10(10): 887–891, October 1965.*

Since "intestinal lipodystrophy" was first described by Whipple[1] in 1907, many misconceptions concerning this remarkable disease have persisted, until recently. The name itself implied that the disease was a disturbance of fat metabolism affecting primarily the small intestine. It was generally believed that the disease was a rarity, that it could be diagnosed only by laparotomy or at autopsy, and that it was invariably fatal. According to recent reports, these beliefs would seem to be erroneous.

Although Whipple himself recognized that the material in the macrophages would not stain as fat, his patient had large amounts of fat in the stool, and he assumed that the disease represented a disturbance of fat metabolism. We now know that this material, which gives the periodic acid-Schiff positive stain (PAS-positive) so characteristic of the disease, is a glycoprotein.[2] It has been known for some time that the disease is not confined to the intestine and adjacent nodes. "Characteristic sickleform PAS-positive cytoplasmic particles have been demonstrated in mesothelial cells of the pleural, peritoneal, pericardial, and synovial lining cells," and also in "the intestine, liver and mesenteric, and peripheral lymph nodes."[3–5] The disease may not be as rare as is generally thought, but merely unrecognized. The diagnosis can be made readily by peroral intestinal biopsy or even by peripheral lymph node biopsy in some cases;[6,7] certainly, it is not necessarily fatal.

Under the electron microscope, the PAS-positive material appears as masses of gram-positive bacilli measuring 0.25 X 1.5μ.[8–10] These structures disintegrate under antibiotic therapy, but retain their staining characteristics until they have disappeared altogether. While these bacteria appear to be invariably present in the untreated patient and in relapse, their etiologic relationship to the disease is yet to be established. To date the disease has not been reproduced in the experimental animal nor has it been transmitted in man.

Diagnosis

Material

Between 1936 and the present, 16 patients with Whipple's disease have been studied here; the cases of 15 have been reported previously.[7, 11–15] One patient was a white female and one a Negro male; the remainder were white males. Their ages at the time of diagnosis ranged between 35 and 62 years. Before diagnosis, the patients had had symptoms other than arthralgia for 6 months to 4 years. In 10 of the 16 cases, the disease was suspected clinically, and the diagnosis was established during life in all except 3. Nine of these patients are alive and well at the present time.

Clinical Picture

The patient is usually a middle-aged white male with a history of intermittent arthritis or arthralgia involving multiple joints over a period of years. However, the actual illness is likely to start gradually with diarrhea; later, gross steatorrhea is accompanied by a marked weight loss and a rapid downhill course. Occasionally, there is no diarrhea and the illness may be accompanied by fever of varying degree. Under such circumstances, the picture is likely to remain unchanged until death unless altered by specific therapy. Determining the date of onset may be difficult, if not impossible. If the joint manifestations are taken as a part of the disease, it has usually existed in mild form for years. Contrarily, if the diarrhea, progressive weight loss, and fever indicate the onset of the disease, it usually has been present for only a few months or years at most. There are no characteristic physical findings. Pigmentation and peripheral lymphadenopathy may be present and the spleen is palpable in a few cases. The dis-

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ease should be suspected in any patient who has a longstanding history of arthritis and later loses a great deal of weight, with or without diarrhea.

Constant Findings

In all 16 patients, arthralgia or arthritis had been present for years. Marked weight loss, 20–100 lb had been noted in every case. Those patients who had had absorption studies all showed impairment of fat absorption. There were diffuse changes in the small bowel, especially in the duodenum and jejunum, in those patients examined radiologically.

The usual laboratory tests are of little value in establishing the diagnosis. The *sine qua non* is the demonstration of impaired absorption of fat. Radiologic changes in the small bowel, although not diagnostic, are highly suggestive of the disease. Actually, the diagnosis cannot be made without histologic study. The simplest method of obtaining a satisfactory specimen is by peroral intestinal biopsy. Finding the characteristic swollen villi filled with macrophages and PAS-positive material establishes the diagnosis.[13]

Treatment

For the first half of this century, once the diagnosis had been established, the family was consoled and the patient sent home to die. In recent years, however, an appreciable number of recoveries following various forms of therapy, especially adrenocorticoid and antibiotics had been reported.[16-18] However, the widespread use of antibiotics in febrile illness and pre- and postoperative management makes it difficult to conclude that those patients reported to have recovered following ACTH administration alone did not receive antibiotics at some time during their illness. In an effort to solve this problem, the case histories of 10 patients who received antibiotics and steroids alone or in combination were reviewed.[15] The 3 who had received antibiotics alone and the 5 who had been given antibiotics and steroids all recovered. The 2 patients who died had been treated with steroids only. No patient relapsed while taking antibiotics. Two had relapses during the administration of steroids only, but recovered after the addition of antibiotics. It was felt, therefore, that antibiotics rather than steroids were responsible for recovery in this group.

Recommended Therapy

All patients should be hospitalized and treated intensively with 1,200,000 U of procaine penicillin G and 1 gm of streptomycin daily for 10 days to 2 weeks. A broad-spectrum antibiotic, tetracycline, is then given by mouth in 1–gm doses daily for the next 10–12 months.

Within days after institution of appropriate antibiotic therapy, the patient experiences a sense of well-being; the appetite returns, the diarrhea ceases, the fever subsides, and a gradual gain in weight is observed. As in other diseases, clinical recovery may by months or years antedate histologic reversion to normal. The PAS-positive material may be present in considerable amounts in the villi as long as 2 years after institution of therapy.[15] Even though PAS-positive material is still present in the villi, the roentgenogram of the small bowel is likely to show reversion to normal within a few months, as is impaired absorption of fat and other abnormal laboratory findings.

None of the patients who received therapy as outlined has experienced a relapse during the period of follow-up, 7 months to 8 years. However, relapses have been observed in 4 patients who received therapy for 6 months or less; all recovered and remained well after more prolonged treatment.

Summary

1. Whipple's disease probably is not as rare as is generally believed, but merely unrecognized. The PAS-positive material in the macrophages of the villi appears to be intact or disintegrated bacilli; however, the etiology of the disease is yet to be established.

2. Suspected clinically, Whipple's disease is diagnosed on peroral small bowel biopsy.

3. Intensive therapy with antibiotics should result in complete and permanent recovery.

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RETROILLUMINATION OF RETINAL VESSELS IN RETINAL EDEMA

Marious K. Jack MD, Seattle, Washington. Am J of Ophth 60(4); 645–647, October 1965*

In three cases of retinal disease of unrelated etiology but with similar clinical findings, direct ophthalmoscopy revealed a significant illumination of the retinal vessels. The presence of this phenomenon was highly correlated with retinal dysfunction and was felt to represent a diagnostic sign of serous retinal edema.

The phenomenon was noted by direct ophthalmoscopy utilizing indirect illumination (proximal illumination) of retinal vessels, principally the arterioles. When the light beam of the direct ophthalmoscope was directed at a point near a retinal arteriole, a striking luminance of the arteriole occurred. Normally, a small amount of indirect illumination of vessels can be elicited if the light source is directed so that the border of its beam is directly adjacent to the vessel. This is especially true in children. It can be demonstrated in adults around the disc where the nerve-fiber layer is thicker. Figure 1 demonstrates the ophthalmoscopic picture of the indirect arteriolar light reflex.

Each of the three cases presented here was characterized by the patient's subjective appreciation of visual loss, demonstrable scotomas and visualization of retinal edema associated with a prominent indirect arteriolar light reflex.

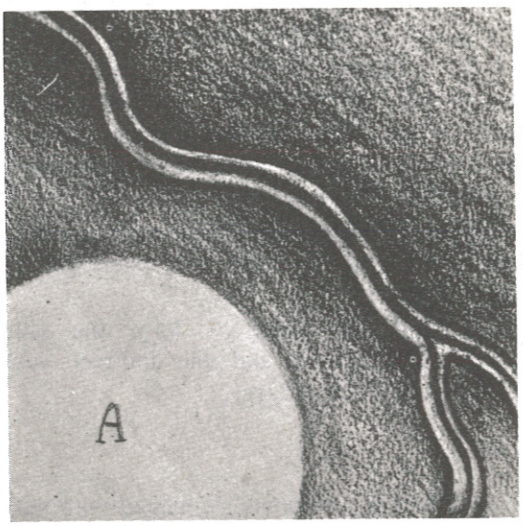

Fig. 1 The indirect retinal vascular reflex is demonstrated by directing the beam of the ophthalmoscope at point (A) and observing the luminance of the adjacent vessel.

Case Reports

Case 1

Unilateral macular degeneration associated with Grade 4 arteriolarsclerosis

A 62-year-old white man complained of an abrupt awareness of blurred vision in his right eye. Examination demonstrated vision to be 6/30 in the involved eye and ophthalmoscopic examination revealed silverwire arteriolarsclerotic changes in the macular branch of the superior temporal branch of the retinal artery. Grade 2 arteriolarsclerosis was noted in the other vessels. There was an absence of the foveal reflex and a slight haziness of the retina superior to and including the macula. Central visual field testing with a 3-mm white target demonstrated a pie-shaped juxta macular scotoma whose apex joined the point of fixation and whose periphery extended to the 15-degree isopter. A bright indirect vascular reflex was easily visualized. Following a week of bedrest, oral nicotinic acid and chymoral medications, there was a progressive improvement in vision to 6/12–3; a reduction in the scotoma to the

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5-degree isopter and a disappearance of the indirect vascular reflex. At three weeks, fine pigmentary changes were observed at the macula.

Case 2

Blurred vision following desensitization with pollen extracts

A 40-year-old woman had begun desensitization for chronic seasonal pollenosis. There were episodes of severe local reactions to the injections in the form of massive edema of the upper arm. Twenty-four hours following a subcutaneous pollen extract injection, the patient became aware of a poorly defined blurred sensation in her left eye. Although her vision was not greatly disturbed, she was concerned and sought attention. Examination revealed vision to be 6/7 in the symptomatic left eye. Visualization of the fundus revealed some minimal indistinctness of the superior retina. The ophthalmoscope revealed a bright indirect illumination of the retinal vessels in that area. Central visual field testing with a 3-mm white test target demonstrated a large scotoma bordering on the fixation area and extending to the 20-degree isopter.

The patient was observed daily, the scotoma eventually disappeared and the indirect vascular reflex was gone in eight days.

Case 3

Mulitple bilateral scotomas associated with strongly positive toxoplasmosis serology and skin test

This most unusual case of a 38-year-old Latin American man concerns progressive loss of central vision first in one eye and then in the other. The patient complained of central visual loss. Central as well as peripheral scotomas were found. Fundus examination revealed a loss of the foveal reflex and an indistinctness to the posterior pole of the retina. Within two weeks a similar process appeared in the other eye. There were no focal chorioretinal lesions to indicate a specific site of disease in either eye. In the presence of a strongly positive skin test to toxoplasmosis and positive hemagglutination serology 1:1024 and following no improvement with a course of systemic steroids, he was treated with Daraprim and sulfadiazine for six weeks. His vision returned to 6/6 bilaterally in two weeks, when disappearance of the scotomas and of the prominent indirect vascular reflex was also noted. Six weeks later fine punctate stippling of the maculas was observed.

Discussion

Serous retinal edema is a commonly made but poorly confirmed observation. It is pointed out that serous retinal edema may be present for a considerable period before it is clinically recognized because of the similarity of the indices of refraction of the edema fluid and the retinal cellular elements.[1]

When disease results in capillary injury to the extent that there is escape of albumin and fibrinogen into the retina as well as cellular breakdown, exudates are formed that are easily visible because of their striking white and dull gray-white color. The edema exudates of commotio retinae and Purtscher's retinopathy are of this type.[2] The watery edema of angiospastic retinopathy is different. Even at the macula where edema is most easily recognized, the changes are more subtle and subjective. The color of the edematous area reveals very little change from normal. There is a characteristic circular or oval light reflex.[3] In general, serous retinal edema is difficult to detect elsewhere. The retina generally appears thicker and more opaque. There is a granular appearance with shimmering and irregular light reflexes. These findings are accentuated in red-free light.[4] At times the minute and parallel nerve fibers are accentuated and thrown into relief in direct illumination. Fundus slitlamp examination, as demonstrated by Pischel, at times demonstrates relucency from the inner retinal layers as well as the outer.[5]

Indirect illumination, ordinarily reserved for slitlamp biomicroscopy, is produced by directing a

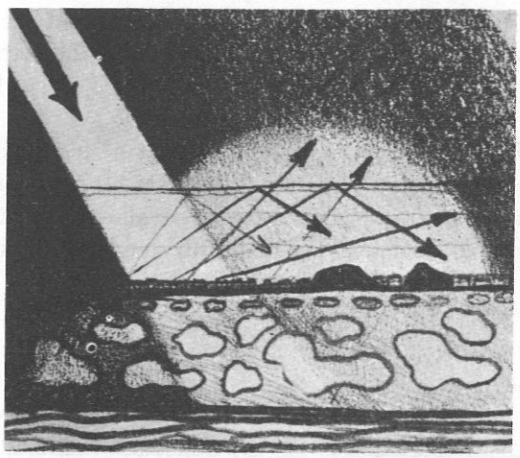

Fig. 2 Indirect illumination of the retina is accomplished by observing the illuminated area adjacent to the direct beam of the ophthalmoscope. Illumination of this adjacent area occurs by scattered and internally reflected light rays.

beam of light on semitransparent tissues, such as the iris. The observer directs his attention adjacent to the direct area of illumination. In these adjacent areas structures not readily seen are illuminated by scattered light and internally reflected light (fig. 2).

Scheie [7] has pointed out that nascent proliferations of the pigment epithelium can often be visualized by this method. He also utilizes indirect illumination of the optic disc to evaluate suspected pallor of not readily evident optic atrophy.

Indirect illumination of retinal arterioles reverses the light pattern seen by direct illumination, which produces a centrally located "light reflex" from specular reflection. With indirect illumination, the central zone of the vessel is dark (fig. 1). Transmission of light through a fluid-filled tubular structure is similar to that which occurs when light passes through two strong plus cylinders axis to axis. The image of the light source becomes a focal line of light whose axis corresponds to that of the cylinders.

When a beam of light is reflected from the choroid through a vessel, a majority of the reflected rays are transmitted through the vessel. They are not visible to the observer at the light source. What the observer does observe is only the internally reflected light, which appears as the two bright outer bands of the vessel in Figure 1. When the reflected rays strike the inner wall of the vessel tangentially so as to overcome the critical angle of reflection, there is internal reflection and this light will be appreciated as the soft red incandescence of the vessels (fig. 3).

A probable explanation for the intensified indirect vascular reflex in serous retinal edema is that, when the vessel is in close apposition to the reflected surface, a relatively small per cent of the light is available for internal reflection. Within certain limits when the vessel is farther away from the reflecting surface more light is available for internal reflection.

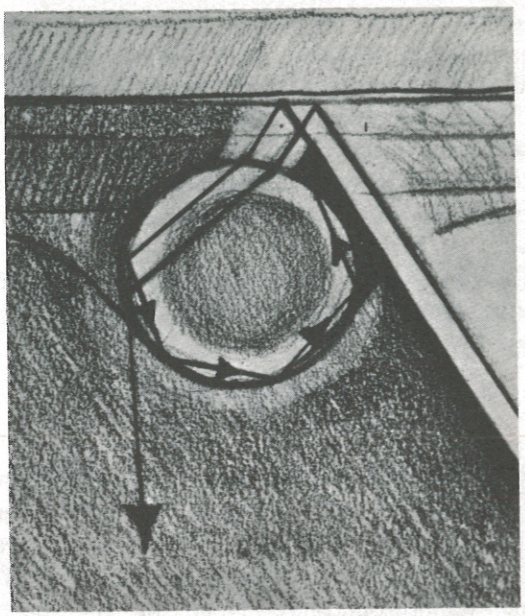

Fig. 3. Diagram to demonstrate the effect of indirect light on a retinal vessel. Here one ray is transmitted through the vessel and another is internally reflected.

Summary

Three diverse cases of retinal disease characterized by retinal edema, scotomas and transient objective and subjective visual loss are presented.

Indirect illumination of retinal arterioles in these cases produced a vascular illumination that was felt to represent a diagnostic sign of serous retinal edema.

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FROM THE NOTE BOOK

SURGEON'S TOOL

The Defense Department has approved a new orthopedic drill which is expected to be used in Service hospitals in the U.S. and overseas, including Vietnam. Tested at Wilford Hall USAF Hospital, Lackland AFB, San Antonio, the cordless electric drill was conceived by Dr. David B. Horner, a prominent orthopedic surgeon with an extensive practice in the Los Angeles area. The Mira Corporation, Los Angeles, developed and manufactures the instrument which carries Dr. Horner's name.

The Horner Surgical Drill, used in bone repair, is powered by a rechargeable, high-energy nickel cadmium battery which does away with electric wires,

connections, foot switches, air hoses and other ancillary equipment necessary with other power drills. A particular advantage for military field and disaster use is that the Horner Drill can be used in areas remote from electric power receptacles because its battery stores more electric energy than is required to power the most extensive surgical drilling procedures.

The drill, with its power pack, weighs four pounds. The power pack will last from three to five years.

PHENOTHIAZINES

Skin-Eye Syndrome

Incidence: Observations were made on 650 mental patients who were receiving psychotherapeutic drugs. Many of the patients had received several courses of various phenothiazines, particularly Thorazine (chlorpromazine). None of the patients showed evidence of skin photosensitivity. However, 103 patients manifested a marked tendency to sunburn, 18 developed marked suntanning resulting in a true brown or bronze color, and 97 acquired a gray or violaceous pigmentation. Slitlamp examinations revealed opacities in the lens and cornea of 33 patients and in the lens alone in 145. Thus more than 25 per cent had eye changes. All but two patients had received Thorazine at one time or another. Duration of Thorazine therapy ranged from 2 weeks to 10 years. The drug had been given in maximum daily doses of 25 to 1500 mg. However, the vast majority of patients had received 400 mg. Thorazine daily for more than two years. Although Thorazine is most often responsible for lens and corneal changes, other phenothiazines are also capable of producing such complications. There is some indication that phenothiazine-induced lens and corneal changes are irreversible.—Barsa et al. (Orangeburg, N. Y.), Am J Psychiat 122: 331, Sept 1965. [For additional information see Clin-Alert No. 63, 1962; Clin-Alert No. 307, 1963; Clin-Alert No. 69, 87, 137, 164, 180, 243, & 296, 1964; Clin-Alert No. 43, 53 & 75, 1965.]

Specialists Opinion: Two ophthalmologists and one psychiatrist joined in this communication. Patients who show skin pigmentation as a result of treatment with phenothiazines often develop granular deposits in the lens and cornea. High-dosage patients may develop such eye changes in the absence of skin changes. The phenothiazine-induced skin-eye syndrome should not be confused with that of retinal changes induced by Mellaril (thioridazine) the two differ radically in onset and pathology.—Brill, Scheie & DeLong, Am J Psychiat 122: 326, September 1965. Republished from CLIN-ALERT No. 270, October 21, 1965, by permission of Science Editors, Inc.

VETERANS ADMINISTRATION MEETING

The Veterans Administration will hold a surgical meeting March 21–22, 1966 at the Boca Raton Hotel, Boca Raton, Florida. Navy Surgeons are invited to attend as guests. Topics on the program include head and neck surgery, esophageal and pulmonary surgery, surgery of the endocrines and wound infections.

SYMPOSIUM ON CURRENT SURGICAL PRACTICES

A symposium on current surgical practices will be held at Walter Reed General Hospital on Monday, Tuesday and Wednesday, 4, 5, and 6 April 1966, as announced in DA circular 350–22 dated 23 April 1965, titled "Education and Training." The Surgeon General of the Army has given his strong support to this seminar. An outstanding program is being arranged and will include recent advances in the fields of general surgery procedures and techniques. Several civilian surgeons of national prominence are included on the program.

You are urged to make application for presentation of papers. Presentations will be limited to 15 minutes with few exceptions. Case reports will also be accepted, limited to 5 minutes. Submit title of your paper, together with an abstract of not more than 50 words, and time desired for presentation, to Colonel C. W. Hughes MC USA, Chief, Department of Surgery, Walter Reed General Hospital, Walter Reed Army Medical Center, Washington, D.C. 20012, with a copy to BuMed, not later than 1 January 1966.

The Symposium is open to surgeons of the Army, Air Force, Navy, Veterans Administration, and also civilians, particularly from the Reserve Corps and National Guard. All are invited and encouraged to attend. Social events will include the wives. There will be a "get-acquainted" cocktail-buffet on Sunday evening, 3 April, at the Walter Reed Army Medical Center Officers' Club.

NAVAL MEDICAL RESEARCH REPORTS

U.S. Naval School of Aviation Medicine, Naval Aviation Medical Center, Pensacola, Fla.

1. A Data Processing System for the Ballistocardiogram: MR 005. 13–7004 Subtask 6 Report No. 12, February 1965.

2. The Effects of Visual Deprivation on Adaptation to a Rotating Environment: MR 005. 13–6001 Subtask 1 Report No. 106, March 1965.
3. Correlational Analysis of Qualitative Data: MR 005. 13–3003 Subtask 1 Report No. 42, May 1965.
4. The K-Coefficient, A Pearson-Type Substitute for the Contingency Coefficient: MR 005. 13–3003 Subtask 1 Report No. 43, May 1965.
5. A Study of Statement Attractiveness Indices Obtained Under Personal and Social Orientations: MF 022. 01. 02–5001 Subtask 1 Report No. 44, July 1965.
6. A Study of the Interpersonal Values Reported by Naval Aviation Pre-Flight Students: MF 022. 01. 02–5001 Subtask 1 Report No. 45, July 1965.
7. Airsickness in Student Aviators: MR 005. 13–6001 Subtask 6 Report No. 1, July 1965.
8. The Relationship Between Past History of Motion Sickness and Attrition From Flight Training: MR 005. 13–3003 Subtask 10 Report No. 8, June 1965.

U.S. Naval Radiological Defense Laboratory, San Francisco, Calif.

1. Presence of Donor Specific Globulins in Sera of Allogeneic Mouse Radiation Chimeras: MR 005. 08–5200, February 1964.
2. Additive Inhibitory Effect of Sublethal X-Radiation Plus Allogeneic Lymphoid Cells on Transplanted Mouse Leukemia: MR 005. 08–1200 Subtask 2, July 1965.
3. Decreased Radiation Mortality in Dogs Treated with Typhoid-Paratyphoid Vaccine: MR 005. 08–5201 Subtask 1, July 1965.
4. Temperature Adaptation of the Growth and Division Process of *Tetrahymena Pyriformis*. I. Adaptation Phase: MR 005. 08–1200 Subtask 9, July 1965.

DENTAL SECTION

Naval Dental Research Reports

To complete the series of Navy presentations at the 43rd General Meeting of the International Association for Dental Research, the last three of fifteen abstracts, concerning the Naval Dental Corps' intramural research program, are reproduced with the permission of the Editor, J D Res. LCDR J. P. Quinn MSC USN (B.S. Bacteriology), has 15 years experience in U.S. Navy Preventive Medicine, and at the U.S. Naval Medical Research Unit #1. He reported for duty at the Dental Research Facility, U.S.N.T.C. Great Lakes in 1963. LCDR W. R. Cotton DC USN (MS, Microanatomy), LCDR W. J. Gorman DC USN and J. R. Lamb DT3 USN conducted their study at the Naval Medical Research Institute. LCDR Cotton is currently stationed at NMRI, and LCDR Gorman is in a Periodontics residency at the U.S. Naval Station, Treasure Island. The other authors' scientific backgrounds were cited in previous issues of this series.

A RELATIONSHIP OF ANTIBACTERIAL ACTIVITY AND THE TOTAL SOLIDS CONTENT OF PAROTID SALIVA TO CARIES DEVELOPMENT

J. P. Quinn and I. L. Shklair, Dental Research Facility, Great Lakes, Illinois.

Nineteen naval recruits with a negative history of dental caries were studied during their first year of service. The ten recruits who developed lesions within the year and the nine who remained caries-free were compared relative to parotid saliva flow rate, its total solids content and its inhibition of Lactobacillus arabinosus ATTC #8014. There was no significant difference in the degree of bacterial inhibition exhibited by the parotid saliva of the caries group and the caries-free group when measured by the two-fold serial dilution of lyophilized parotid saliva in Rogosa Broth. Calculation made of the milligrams per milliliter total solids of parotid saliva in the highest dilution exhibiting no growth after twenty-four hours incubation indicated that the parotid saliva of the caries group contained essentially the same amount of inhibitory substance as the parotid saliva of the caries-free group. There was no significant difference in the amount of solids secreted per milliliter between the caries group and the caries-free group, however, the milligrams total solids per minute flow rate was seventy per cent greater for the caries-free group.

PULP RESPONSE TO CAVITY DRYING IN RAT TEETH

W. R. Cotton, W. J. Gorman and J. R. Lamb, Naval Medical Research Institute, Bethesda, Md.

The immediate response of the pulp was evaluated following drying of a cavity by a stream of temperate air for 5 minutes. Thirty-five maxillary first

molar teeth, 15 control and 20 experimental, were used. All cavity preparations were made under air-water spray with a wire-twist drill revolving at 1300 ± 40 rpm. All animals were sacrificed immediately upon completion of a test and control cavity in each rat. All 20 air-dried cavities showed odontoblast nuclei displacement into the dentinal tubules. Thirteen of 15 non-air-dried cavities did not show nuclei displacement into the tubules. This would seem to indicate that one immediate response of the pulp to the air-stream was displacement of the odontoblast nuclei into the dentinal tubules. Within the dentinal tubules of the experimental teeth, vacuoles were seen within the displaced nuclei. These may be degenerative changes. Increased number of depth of displaced nuclei occurred in tubules associated with the cavity margin, i. e., marginal displacement, in 9 of 22 teeth which had ectopic nuclei. A significant ($P < 0.01$) correlation was found between the direct measurement of the cavity depth and both number ($r = 0.589$) and depth ($r = 0.585$) of nuclei displacement into the dentinal tubules. The tubular measurement of remaining dentin was significantly correlated to the number ($r = -0.556$, $P < 0.02$) and depth ($r = -0.456$, $P < 0.05$) of nuclei displacement. The direct measurement of remaining dentin was not significantly correlated to the number ($r = -0.403$, $P > 0.05$) and depth ($r = -0.377$, $P > 0.10$) of nuclei displacement.

A SUGGESTION THAT COLLAGEN IS A THIRD CLASS OF PROTEIN WITH REGARD TO ITS LOW TEMPERATURE LUMINESCENCE

K. C. Hoerman, S. A. Mancewicz and A. Y. Balekjian, Naval Medical Research Institute, Bethesda, Maryland.

Total emissivity of powdered dentin collagen at 89° K following irradiation with ultraviolet light at 270 mμ revealed fluroescence maxima at 308 and 395 mμ while phosphorescence occurred in a wide band whose maximum was at 420 mμ. The singlet-triplet transition in this tissue was related to the 308—420 mμ intercombination leaving the fluorescence at 395 mμ without a detectable triplet state emission. Diminished photomultiplier response at higher wavelengths could account for this. Normal acid-extracted rat skin collagen had a single fluorescence maximum at 300 mμ with phosphorescence at 395 mμ. It was implied from these data that an impurity secondary activation site existed in dentin collagen. A comparative study was undertaken using as models RNase (phenylalanine → tyrosine emission), lysozyme and human serum albumin (phenylalanine → tyrosine → tryptophan emission). The shape of the total emission curves and their maxima suggested that collagen dissipates absorbed energy from a third order of luminescent center(s).

TREATMENT OF LARGE CYSTS OF THE JAWS IN CONSIDERATION OF POTENTIAL NEOPLASIA

R. Weinstein, J Oral Surg 23(6): 489–496, September 1965.

The author discusses the different methods of treating large cysts of the jaw. The two conservative approaches (1) the Partch or marsupialization operation and (2) the tube technic are described, as well as complete enucleation. The objection to the marsupialization and tube technic is that the patient is denied a complete microscopic examination. Such microscopic examinations have become more important with the increasing number of reports of neoplastic development in the walls of cysts. Objections to enucleation revolve around the possibility of fracture or injury to adjacent or associated structures.

The author then presents three cases treated by enucleation with primary wound closure. Results were satisfactory with no untoward effects, and the microscopic findings in two of the three patients gave ample justification for the method of treatment. In all three cases the clinical diagnosis was dentigerous cyst. Microscopic examination in just one case revealed merely a dentigerous cyst. In the second case the pathologist's diagnosis was dentigerous cyst with mural ameloblastoma arising from the second molar. The third case was a dentigerous cyst with ameloblastoma arising from the first molar.

The author then reviews the literature describing the many reported cases of ameloblastomatous, adenoma-like and carcinomatous changes in the walls of these cysts. With a clinical diagnosis of dentigerous cyst, the surgeon who elects a marsupialization or tube technic must recognize the possibility that he is allowing a neoplasm to grow while he is waiting for the cyst to shrink or for the defect to fill in. Complete enucleation permits complete microscopic examination; and early diagnosis of neoplasm permits optimal treatment. (Abstracted by: CDR H. S. Kramer, Jr., DC USN, U.S. Naval Hospital, Chelsea, Massachusetts.)

DISEASES OF THE TEETH IN 1578

One of the earliest known doctoral dissertations devoted to dentistry is that of Peter Monau, written

in 1578. The thesis "De Dentium Affectibus" was presented to the faculty at Basel on February 20, 1578. Monau had studied at Wittenberg, Heidelberg and Padua before coming to Basel.

Monau was born on April 9, 1551, the son of a patrician family of Breslau, and died while serving as physician to Kaiser Rudolph II in Prague on May 12, 1588.

Monau said that the tooth was hard at its functional surfaces, and softer at the roots. He found no nerves in teeth and described the periosteum as the most sensitive region. In addition to their principal masticatory function, Monau said that teeth aided in speech. Monau believed that certain diseases of teeth were inherited; he ascribed decay to ingestion of food too hot, too cold or too hard. He first described what is today recognized as pulpal polyps.

For pain, Monau prescribed narcotics and local application of opium. Opium was to be applied in the form of a mouthwash or dissolved in milk, oil or wine. Monau cautioned against frequent intake of sweets because, he said, the teeth blackened and became susceptible to decay. He suggested frequent cleaning with toothpicks of wood rather than metal.

Although many of Monau's comments and descriptions have long since been modified or discarded, when viewed against knowledge in the sixteenth century, the dissertation represented an excellent review and discussion. (Lorber, Curt Gerhard. Universitatsstrasse 10, Heidelberg 69, Germany. Peter Monau's Dokotordissertation Uber Erkrankungen der Zahne aus dem Jahre 1578. Zahnarztl. Mitt. 53:764–765, Sept 1,, 1963. Dental Abs 10(7): 426, July 1965. Copyright by the American Dental Association. Reprinted by permission.)

PERSONNEL AND PROFESSIONAL NOTES

NAVY EXCHANGES COOPERATE IN PREVENTIVE DENTISTRY PROGRAM. The Commanding Officer, U.S. Navy Ship's Store Office, Brooklyn, New York recently distributed a notice to all activities operating Navy Exchanges requesting that they display signs promoting the use of stannous fluoride dentifrices. A sample sign was enclosed carrying the following message:

Receivers of
NAVY TOOTH DECAY
PREVENTIVE TREATMENTS
Are reminded that only
STANNOUS FLUORIDE TOOTHPASTES
INSURE FULL BENEFITS
of the program

The notice encouraged display of a sign in each area where dentifrices are sold for approximately one week out of each month. It was considered that signs of this nature would have a greater impact on customers if they were displayed intermittently rather than on a permanent basis.

RED CROSS VOLUNTEER DENTAL CLINIC ASSISTANTS. Programs for Red Cross Volunteer Dental Clinic Assistants in Armed Forces dental facilities have been developed in conjunction with the national Headquarters, American National Red Cross. Pilot studies in naval activities have been highly successful. The ladies may perform as clerk-receptionists or as chairside assistants, depending on their level of training. This program is believed especially appropriate and desirable at foreign shore and at CONUS activities which have been designated remote for dependent dental care. Many dependent ladies seem to volunteer for this program because it gives them the satisfaction of contributing to the oral health and welfare of their own families. Others volunteer in part because it gives them opportunity to gain experience which will be useful in gaining employment as a dental assistant to a private practitioner, in the area of her husband's next duty station. Dental officers may obtain additional information by a letter addressed to the Chief, Bureau of Medicine and Surgery (Attention Code 611).

DENTAL OFFICER PRESENTATIONS. CAPT K. C. Hoerman DC USN, Head, Biochemistry Division, Dental Research Department, NMRI, participated in the Seminars on Connective Tissues, 10-16 October, Rheumatism Research Unit, University of Vermont, College of Medicine, Burlington, Vermont. He discussed "Molecular Luminescent Phenomena in Normal and Lathyritic Rat Skin Collagen." CAPT Hoerman recently relieved CAPT H. W. Lyon as Head, Research Branch, Dental Division, Bureau of Medicine and Surgery, and Dental Projects Officer, Medicine and Dentistry Branch, Office of Naval Research.

CAPT P. J. Boyne DC USN, Director, Dental Research Department, NMRI, lectured on "Research in Oral Surgery," at the Surgical Seminar, Georgetown University, Washington, D. C., on 30 September 1965.

LCDR W. R. Cotton DC USN, Dental Research Department, NMRI, was a guest of the University of Alabama, School of Dentistry at the "Workshop on the Biology of the Dental Pulp Organ," 28 September to 1 October 1965. Dr. Cotton presented a paper entitled, "New Techniques and Their Application to the Study of Pulp Tissue: Pulp Response to Cavity Preparation as Studied by the Method of Thymidine-H ^{3} Autoradiography."

LIST OF NEWLY STANDARDIZED ITEMS AVAILABLE FOR ISSUE

FSN	NOMENCLATURE	UNIT	PRICE
6520–226–0914	Wax, Dental, Utility 60 Ropes, 350 Gm:	BX	1.90
6520–787–2888	Wheel, Abrasive, Straight Handpiece Sq. Edge 1/2 X 1/4 inches, No. 303, 6s:	EA	3.10
6520–787–2890	Wheel, Abrasive, Straight Handpiece Round Cone, 1/2 X 3/8 inches No. 300 6s:	EA	2.50
6520–880–6842	Wheel, Abrasive, Aluminum Oxide Straight Handpiece, Denture Trimming Cone, 3/8 by 3/4 inches 6s:	EA	3.20
6520–880–6843	Wheel, Abrasive, Aluminum Oxide, Straight Handpiece, Denture Trimming Cone, 3/8 by 3/4 inches 6s:	EA	3.20
6520–880–6844	Wheel, Abrasive, Aluminum Oxide, Straight Handpiece, Denture Trimming Bud.; 1/2 by 5/16 inches 6s:	EA	3.20

PREVENTIVE MEDICINE SECTION

VARIABLE EPIDEMIOLOGY OF STREPTOCOCCAL DISEASE AND THE CHANGING PATTERN OF RHEUMATIC FEVER

G. H. Stollerman, A. C. Siegel, E. E. Johnson, Modern Concepts of Cardiovascular Disease 34(10): 45–48, Oct 1965.

Decline in Overt Rheumatic Fever

It is extremely difficult to determine accurately the incidence of acute rheumatic fever in large civilian populations. Few studies are available to support with convincing data the impression of many clinicians that rheumatic fever is becoming less frequent and severe in North America and Europe. Mortality statistics reveal a striking decline in deaths due to acute rheumatic fever, STAMLER, 1962. In many cities of the United States, convalescent hospitals and homes for children with rheumatic fever have closed their doors or changed their admission policies to include patients with other related diseases. Some large pediatric hospitals which once reserved a special section of their medical wards for rheumatic fever patients now distribute the sporadic rheumatic case load among the general medical beds.

It is becoming more difficult to find cases of Sydenham's chorea, and fulminating, fatal rheumatic pancarditis has become relatively rare. In many North American clinics, the school-age child with a huge heart, bulging precordium and greatly congested liver is now more likely to have congenital heart disease than advanced rheumatic heart disease. A recent large-scale survey has shown that congenital heart disease is at least as common as rheumatic heart disease in the elementary school population, Miller, et al, 1962.

Change in Streptococcal Epidemiology

If there has been a decline in the incidence and severity of rheumatic fever, one might expect this to be related to a change in the epidemiology of streptococcal disease. Although there has been a marked decline in epidemic streptococcal sore throat and scarlet fever, group A streptococci have remained ubiquitous in school children's throats. Wherever ex-

tensive throat culturing has been made, it has been possible to isolate these organisms in approximately 40% of patients in this age group during the course of the school year, although the rate varies greatly in any given season, year, population, or geographical location. The prevalence of throat cultures positive for group A streptococci in some populations in which little rheumatic fever has been found has caused surprise and confusion. Some confusion stems from a lack of appreciation of the difficulties in distinguishing among (a) streptococcal and viral infection on clinical grounds alone, (b) carriers of group A streptococci and those actually infected, and (c) the severity of the streptococcal disease measured, not by clinical symptoms alone, but by other significant parameters, such as the magnitude of the immune response and the duration of convalescent carriage of the infecting organism. The latter two features of streptococcal infection have been shown to be related most closely to the attack rate of rheumatic fever, RAMMELKAMP, 1958, STETSON, 1954.

The magnitude of the immune response and the duration for which organisms persist in the throat during convalescence are related to the virulence of the streptococcal strain causing the infection. The two most important factors related to virulence of group A streptococci are the type-specific M protein surface antigen and the capsule of hyaluronic acid, both substances which confer upon the streptococcus the property of marked resistance to phagocytosis, LANCEFIELD, 1962.

In military epidemics of streptococcal pharyngitis, more than 90% of the group A strains isolated from patients with exudative pharyngitis may be typable with specific anti-M protein antisera, and usually one type predominates. Furthermore, such predominant, epidemic types are often richly encapsulated and may grow on solid media as large, mucoid colonies. In untreated patients, such strains may persist in the throat for as long as 4 weeks in 80% of individuals, and 85 to 90% of the individuals thus infected may show a vigorous response in antistreptolysin O, or other streptococcal antibodies.

The relative mildness of the sporadic streptococcal disease which may be encountered in a large metropolitan population of school children from a relatively low socioeconomic group is demonstrated by recent studies in Chicago, SIEGEL, et al, 1961. In patients with pharyngitis associated with a throat culture positive for beta-hemolytic streptococci, 85% harbored strains belonging to group A, but in less than half of these were the organisms typable with anti-M serum and in only half was the illness associated with an increase in antistreptolysin O titer. Furthermore, the magnitude of the antibody responses was considerably less than that observed in cases of exudative pharyngitis in military populations.

Clinically, of those patients with pharyngitis who had group A streptococci in their throats, only 40% had pharyngeal exudate, 30% had fever greater than 38.2C (101F) and only 16% had a white blood cell count greater than 12,000/cu mm. Therefore, among 608 patients who had a sore throat associated with throat cultures positive for beta-hemolytic streptococci, there were only 95 who had the complete picture of exudative pharyngitis associated with group A streptococci and an increase in ASO titer. Only 81 patients in this group carried the infecting organism in their throats for a period longer than 21 days after the infection subsided. Less than one in every six patients, therefore, would have been considered to have an infection comparable in magnitude to the infections observed in military epidemics which have been associated with rheumatic fever attack rates of 3% or greater.

Strain Virulence and Epidemiological Studies

An understanding of the relation of strain virulence of group A streptococci to the incidence of rheumatic fever is essential if confusion is to be avoided in epidemiological studies and community projects now in progress in the United States and in several foreign countries. Information about streptococcal infections limited to the identification of group A streptococci in the throat of a given population is not adequate for a full appraisal of the epidemiology of the streptococcal disease in question when the latter is sporadic. The routine throat culture is still an invaluable tool with which the clinician may *exclude* the streptococcal etiology of a sore throat when the cultures are negative. When they are positive, he may identify a succession of exudative pharyngitides as an incipient epidemic of streptococcal disease. The results of routine throat culturing of *healthy populations* can be misleading, however, if no further information is obtained other than the presence or absence of beta-hemolytic streptococci. Routine throat culturing of children by school nurses or in other community programs involving populations in which streptococcal disease is not epidemic may give misleading information.

The above considerations argue strongly for the

continued availability of typing sera for M protein. The appearance in any population of a large number of strongly M positive strains, particularly when all or most are of one type, is indicative of rapid human passage of a strain of high virulence and suggests conditions under which rheumatic fever should appear with greatest frequency and severity. Unfortunately, there is a tendency for some streptococcal reference laboratories, particularly in Europe, to stress the identification of streptococcal strains by Griffith's slide agglutination test, which is made with antisera for T-antigen typing. Although this method will identify by another marker (the T antigen) streptococcal strains which have lost M antigen and will thus yield a high percentage of "typable" strains, the presence of T antigen bears no relation to streptococcal virulence and offers little or no help in the particular problem of determining the potential danger or clinical significance of a given streptococcal strain. Recent studies have shown that group A strains lacking M protein and capsules cannot kill hypogammaglobulinemic animals, such as baby germ-free mice, and cannot resist phagocytosis by the blood of the new-born colostrum-deprived piglet, an animal virtually free of antibodies, STOLLERMAN, et al, 1965.

It has required a good many years of painstaking research to identify accurately the kind of streptococci most dangerous to man, LANCEFIELD, 1962. If the approach to the control of diseases due to this agent is to progress effectively, increasing sophistication in bacteriological procedures for identifying the properties of these organisms will be required, as well as a better understanding of the problem by the clinician who must interpret the results of the laboratory report.

Value of Throat Cultures to the Practitioner

The above discussion should not be interpreted to imply that the throat cultures of patients with sore throat are of no value to the practitioner. The detailed bacteriological study of group A streptococcal strains is of importance in the thorough appraisal of the epidemiology of streptococcal disease. A selective culture for the simple identification of beta-hemolytic streptococci on a blood agar plate is of great value to the clinician faced with the decision of whether or not to treat a patient with sore throat, and if so, how vigorously. In the first place, a negative culture virtually excludes the need for antibiotics except in certain rare instances (e.g., where diphtheria may be suspected). Negative throat cultures in a succession of patients with *exudative* pharyngitis strongly suggest outbreaks of adenovirus, or at least some viral agent capable of producing a clinical picture of sore throat indistinguishable from streptococcal pharyngitis.

A sporadic positive culture is more difficult to interpret. If exudative pharyngitis is associated with strongly positive cultures for beta-hemolytic streptococci, there is usually no argument. Moreover, if several such cases are observed in succession, the clinician can promptly recognize an incipient epidemic, or a succession of passages of a strain, throughout a family or a school. By the routine use of the throat culture, the clinician becomes aware of the nature of the pharyngitis prevalent in his practice at different seasons and this strongly influences his decision as to whether or not treatment should be administered.

Treatment of the patient and his intimate contacts when streptococcal disease becomes prevalent will promptly interrupt rapid strain passage and will lead to a decrease in strain virulence. Thus, the vigilance of the practitioner and his routine use of the throat culture are the best protection presently available against epidemic streptococcal disease and if properly applied should lead to a progressive decrease in the prevalence of virulent streptococcal strains and to a continued decline in the incidence of rheumatic fever.

BOUTONNEUSE FEVER

During April and May 1963 an outbreak of Boutonneuse fever in U.S. personnel was reported by a naval training command, then designated as a U.S. Naval Air Station. Twelve cases were seen and treated at the Station Hospital before preventive measures could be instituted.

In April 1964 preventive measures were initiated prior to the occurrence of any cases of Boutonneuse fever in American personnel. Unfortunately, 2 cases were incubating and diagnosed 6 days after preventive measures had been implemented.

In April 1965 preventive measures were instituted one week earlier than in 1964 and this effort proved fruitful with 1965 being the first year without the incidence of Boutonneuse fever in American personnel in 3 years of record.

Preventive measures for the control of the vector, the brown dog tick, ***Rhipicephalus sanguineus*** (Latr.) are as follows:

a. During the month of April, spraying with 1% lindane emulsion, is conducted of all yards of homes

rented by American personnel in the nearby cities. (No local pest control program is available).

b. Spraying of all yards, playgrounds, athletic fields and picnic area aboard the naval training command in April with 1% lindane emulsion.

c. Establishment of a dog dip tank, containing 0.5% lindane emulsion, at the station kennels, available on a year-round basis, for the control of Canine ectoparasites.

d. Providing an ample supply of tick and flea powder for canines and felines through Navy Exchange retail store and the Animal Clinic.

e. Cutting and burning of vegetation in areas that are uninhabited but where persons or children travel or play.

f. Through indoctrination lectures and on a continual basis through base news media, a public information program was instituted to apprise personnel of the necessity for the control of ticks and other ectoparasites.

Due to proven effectiveness of the tick control program, it is projected that a similar program be conducted continually. The paramount phase being the residual application of insecticide to yards, etc., during the first two weeks of April or as soon as the increase of tick population is recognized.—PrevMed, BuMed.

CIGUATERA POISONING

U.S. Dept of HEW, PHS, 1 Sept 1965 Press Release.

Research on poisons found in or produced by edible marine life has led to the isolation of and discovery of an antidote for an ancient poisonous substance found in tropical fish around the world.

Existence of the poison has been known for centuries, but until recently there has been no antidote because of the unknown chemical composition of the material and how it works in the body.

Two professors of zoology and chemistry at the University of Hawaii's Marine Laboratory, have isolated ciguatera poison (sigwaterra), which produces a disabling and sometimes fatal disease contracted by eating various kinds of tropical fish.

A member of the team was the first person to define the action of the poison using experimental animals.

Experimentation with the poison on laboratory animals showed that it operated by inhibiting enzymatic action, the specific enzyme being cholinesterase. This is the same action manifested by the organo-phosphate pesticides used widely in this country and throughout the world. The Hawaii investigators tried drugs used for the treatment of organo-phosphate poisoning and found that one of these, Protopam chloride, used in rats and mice previously poisoned with the ciguatera toxin, was an effective antidote if given soon after the onset of symptoms.

The action of the antidote has been proven effective in laboratory animals and has kept animals alive that had been given over twice the normal lethal dose of ciguatera poison. In 1 case where the drug was given to humans, it was credited with saving a life, but appeared to have serious side effects—flushing, high blood pressure, feverishness, rapid pulse, and broncho-constriction. Two of the patient's friends, who had eaten the same fish at the same party, died.

In 1964, in Hawaii, 8 persons were stricken after eating a home-cooked dinner consisting mainly of a stew containing several types of fish, including the entrails and liver. The attending physicians stated that they advocate the use of Protopam chloride if an early diagnosis of ciguatera fish poisoning can be made.

Symptoms are marked by restlessness, apprehensiveness, profuse sweating, a high white blood cell count and diarrhea, followed by involuntary twitching of muscles throughout the body, labored breathing, and the absence of deep tendon reflexes. Ciguatera is considered to be the least virulent form of fish poisoning, or ichthyosarcotoxism. The mortality rate is about 2 to 3%. Complete recovery is a matter of weeks or months.

Ciguatera poison still has not been precisely defined chemically, but it is known to be found in a number of carnivorous fish, including the red snapper, the grouper, moray eels, barracuda, lagoon sharks, jacks and surgeon-fish. The toxin appears to be passed through the food chain by the food fish of the carnivores, the smaller reef fish. The smaller fish appear to obtain the toxin from feeding on a yet unknown alga, but it does not harm them.

It is found in extremely small concentrations in the fish so that scientists could isolate only 1 part by weight in approximately 10 million parts of fish. It is known that ciguatera toxin is stored in the fish for long periods of time and is found in much greater concentrations in the liver, gonads and other viscera than in the flesh. The toxin in the viscera is many times—perhaps as much as 50 times—more concen-

trated than in the flesh. Nevertheless, the flesh may be sufficiently toxic to cause coma or death.

The team first isolated the substance responsible for ciguatera poisoning from the red snapper. Although identical material has been found in other species, all those implicated in known cases of the poisoning were caught in restricted areas around coral reefs of the tropics. The same species of fish may be completely safe if caught a few miles away from the toxic section of the coral reef.

The poison has been reported found in such fish throughout the tropical belt—in the Caribbean, the archipelagoes of the tropical Pacific, and from Madagascar across the Indian Ocean. It has also been found in fish in the Mediterranean. Fish are a valuable source of protein for certain population groups in these areas, where dietary protein deficiency is a problem.

Ciguatera poisoning was responsible for 3 outbreaks reported in scientific journals in 1963 and 1964 as occurring in Jamaica and involving 61 persons who ate barracuda. An outbreak in Florida in 1962 with similar but mild symptoms, was attributed to shellfish. Ciguatera poisoning was suspected but the substance was never specifically identified. "Public Health Reports" of Sept 1956, reported a series of outbreaks in Florida of fish poisoning caused by eating barracuda, but again ciguatera poison was not specifically identified.

Ciguatera fish poisoning incidents are recorded at least as far back as the discovery of America. Conquistadores in Haiti and Cuba, who followed Columbus to America, found local game scarce and turned to the sea for food. They ate fish, crustaceans, mollusks, and an easy-to-capture marine snail now known as Burgo (*livona pica* Linnaeus). Burgo was the source of numerous gastrointestinal and nervous disorders among the Conquistadores, who gave the name of Cigua to the snail and called the disorders Ciguatera.

Burgos are still an important part of the diet in the remote areas of the isolated islands of the French Antilles and continue to be the source of ailments analagous to those described by chroniclers in the Caribbean in the 15th and 16th centuries.

According to Philip Helfrich, a marine biologist at the University of Hawaii Marine Laboratory, who published a report in 1961 entitled "Fish Poisoning in the Tropical Pacific": "Ciguatera poisoning appears to present the most serious fish poisoning problem in the Pacific at the present time, primarily due to its widespread occurrence and the multitude of highly esteemed food fishes that may harbor the undetectable ciguatera toxin."

Scattered reports over the past 350 years indicate that the outbreaks have occurred in the following island groups: Ryukyu, Mariana, Caroline, Marshall, Gilbert, Ellice, Fiji, Samoan, Phoenix, Society, Tuamotu, and Marquesas, as well as in New Caledonia, the New Hebrides, and tropical Australia. In the 1940's outbreaks were reported in the Line Islands and Midway Island; and in the 1950's, Johnston Island and Oahu Island in Hawaii.

TICKS

The Zoology Laboratory at the U.S. Naval Medical Research Unit Number Three, Cairo, Egypt, housed in a group of unpretentious buildings, is a scientist's treasure trove. Dr. Harry Hoogstraal heads a well-organized group supported by specialists, each contributing in his own field. By a highly selected process, throughout the years he has collected and trained a group of excellent technicians who perform exact and meticulous duties with a high standard of proficiency. These technicians, with limited academic backgrounds, have acquired skills through training and thus have become major contributors to the output of this productive laboratory.

Through the years the laboratory at NAMRU–3 has accumulated specimens of ticks—particularly from Africa and the Near East—from all over the world, and the collection now represents one of the finest available. Because of Dr. Hoogstraal's reputation as a scientist, and his cooperative spirit, his colleagues have contributed much to this collection.

The collection of ticks is not a museum collection but rather a working tool for the principal investigator and his workers. Each specimen is carefully labeled as to name, type, stage of development, sex, and is given a reference number referring to information in a cross-index. For the past 12 years, this writer has watched with interest the collection grow from an ordinary but excellent and systematic filing into its magnificent present stature. The material has been the source of information for more than 100 published papers on ticks as well as for the book, *Ticks of the Sudan*, and will be used in 3 more volumes which are under preparation.

Throughout the years, Dr. Hoogstraal has systematically accumulated reprints of various publications on ticks, and their taxonomy, distribution, ecology, and role as vectors in human and animal diseases. From this collection, although incomplete but containing most of the worthwhile references in

the field, Dr. Hoogstraal is developing an annotated bibliography, which will systematize this vast amount of literature and facilitate its use in the preparation of manuscripts. Two books on ticks and tick-borne diseases, are being planned. This bibliography, now being worked out as to subject, author, geographical area, diseases and vectors, should provide investigators with a ready reference covering important fields and should save a large amount of library time for those interested in specific aspects. This coordination of knowledge will prove as useful as the many fine original pieces of investigation that have been reported by this laboratory.

Another collection, constantly being enlarged, is that of specimens of mammals from Egypt and the Sudan. The records and specimens are carefully coordinated as to geographic location and the ectoparasites associated with them. These substantiate and afford background for ecological studies in intermediate hosts in development of the ticks and the animals' potential reservoirs of tick-borne diseases. Dr. Hoogstraal is particularly fortunate in having Sobhy Gaber, more commonly known as "Soapy," (an Egyptian laboratory technician) who has a green thumb when it comes to raising ticks. New specimens are brought to the laboratory and the life cycle carefully followed from egg to adult. At each stage of development, the specimens are carefully observed and their descriptive characteristics recorded, so that both adult and immature stages of the specimens may be readily identified.

During the rearing process, specimens are selected and slides are made. NAMRU–3 records of adult specimens and slides on both immature and adult forms. Again, the careful, thoughtful planning of passed years is demonstrated in the orderly manner in which this material is filed available for use in identifying specimens received at the laboratory.

Studies on several new forms of avian plasmodia are being carried out. Cooperative studies are conducted by Dr. Hoogstraal in conjunction with investigators from the UK, US, India, Asia, Africa and in other countries. He is cooperating with Dr. Harold Trapido of the Rockefeller Foundation in preparing a book on *Haemaphysalis* ticks.

A collection of Egyptian "fat rats" (*Psammomys obesus*) was made famous because of their susceptibility to diabetes. Each week these much-desired animals are collected and shipped to laboratories all over the world.

One of the services the NAMRU–3 laboratory provides is the translation of Russian articles on ticks and tick-borne diseases. This literature, which is obtained through purchase and exchanges of reprints with Soviet investigators, is translated into English by a translator attached to the Unit and provides usable documents for the western world. These translations are provided to a large distribution through ONR London. Approval and appreciation of this service is repeatedly expressed by its many recipients.

One cannot leave Dr. Hoogstraal's laboratory without noting the artistic and accurate illustrations which support the detailed taxonomic descriptions so necessary in the preparation of manuscripts.

Dr. Hoogstraal maintains an unusual library of publications on the fauna of Egypt and the Nile Valley. This personal library contains old and rare publications closely related to his work, but always available in many larger libraries.

It is from this unpretentious, well-staffed, excellent small group of laboratories that so much fine material comes on the nature and importance of this special group of disease vectors. (CAPT J. R. Kingston MC USN, Office of Naval Research, Washington, D. C.: formerly of the office of Naval Research Branch, London.)

FLEAS
A CONTINUING PROBLEM

Waldron, W. G., Los Angeles County Hlth Index, 38th Rpt Wk, ending 25 Sept 1965.

Fleas, as vectors of bubonic plague have played an important part in the history of mankind. They are also a continuing problem as a source of annoyance to both man and animals.

The fleas most closely associated with man and his pets have not been directly implicated as serious vectors of disease. However, all arthropods that feed upon man must be considered as being of potential public health significance.

In Southern California, the cat flea, *Ctenocephalidis felis,* is the most common variety, and the one which represents the greatest summer-time nuisance to man. Occasionally the flea involved will be the dog flea, *C. canis,* or the human flea *Pulex irritans.* These fleas are frequently, but incorrectly, called "sand fleas." They receive this designation because their eggs drop from the host animal onto the ground where they complete their life cycle. Household pets are the common hosts. The floor or ground is the usual harboring place for fleas. They can be easily transported by pets, or clothing, to beds,

chairs and sofas. From the soil, floor or furniture they may leap upon a man or pet to feed.

The life cycle of the flea passes through four steps of development; the egg, the larvae, the pupae and the adult. Eggs may be laid upon the host animal, then subsequently drop to the floor or soil where they hatch into larvae. The larvae spin tiny cocoons in which they change into pupae and then into adults. Upon emerging from the cocoon, the adult flea is ready to feed upon some warm blooded animal.

Fleas subsist upon the blood of their host, be it man, bird or animal. On man, the flea usually feeds upon the ankles although his bites might eventually cover the entire body. The flea is a rapacious feeder and may inflict several wounds before his appetite is satisfied. The reaction to the bite varies with individuals and in some, may result in considerable discomfort and excessive itching.

Pet owners who have been on a vacation frequently return to find their home overrun with fleas. This situation may be explained by the fact that the adult flea can live for several weeks without food. The return of the home owner represents a meal to the hungry fleas, both old and newly hatched, and at such times, they apparently all desire to eat at once.

Techniques and insecticides * are available to abate a flea problem. The usual procedure is to deflea the pet, spray the yard with an insecticide and vacuum-clean the house and furniture. It must be borne in mind that the pet, the house and the yard must all be treated the same day. This treatment must be repeated one week later.

* NOTE: For information, call your nearest preventive medicine unit, disease vector control center, or naval district public works office. (Vector control section, PrevMedDiv)

KNOW YOUR WORLD

Did You Know?

That a serologic test to aid in the diagnosis of cases of suspected amebic liver abscess was made available to the Virginia State Health Department Laboratory by the Laboratory Branch, Communicable Disease Center, Public Health Service, Atlanta?

Results obtained with the indirect hemagglutination test indicate that this test is sensitive and specific for extra-intestinal amebiasis. Of 127 cases of amebic liver abscesses studied, 117 were positive in high titers.

Physicians are encouraged to submit specimens, accompanied by detailed histories, from suspected cases of extra-intestinal amebiasis to the State Health Department Laboratory for evaluation of this test. (1)

That Parkinson's disease takes more than 28,000 lives a year in the United States with about 40,000 new cases occurring annually? (2)

That the whole territory of Afghanistan was declared free of cholera by notification to the World Health Organization on 3 October 1965?

When the presence of cholera was noted on 22 July 1965, the disease had not been reported since December 1960. 218 cases and 55 deaths were reported, all in the northern provinces. The epidemic was due to both classical cholera and cholera El Tor. (3)

That the 1964 outbreaks of rubella (involving 8 states) constituted the largest epidemic recorded since 1935 (23 states involved)?

Because of the national importance of this disease, particularly in women in the first trimester of pregnancy and the resultant congenital malformations in newborns, the Biennial Conference of State and Territorial Epidemiologists of the USDHEW Public Health Service has recommended that rubella be placed on the list of nationally reportable diseases, effective 1 January 1966. (4)

That an outbreak of poliomyelitis, 47 cases through mid-September 1965, occurred in San Pedro area of Honduras?

The date of onset of the first cases is not known. In the epidemic area, 59,000 children were given Salk-type vaccine; 23,000 under age 9 remain to be inoculated. Pending determination of the polio-virus type, health authorities are recommending use of the trivalent vaccine. The World Health Organization has supplied 100,000 doses. The Honduras Ministry of Health is requesting an additional 200,000 doses from Mexico. (5)

That poinsettia leaves and mistletoe berries are poisonous if eaten?

A single poinsettia leaf can kill a child and both children and adults have died from eating mistletoe berries, according to the National Safety Council. (6)

That the nation's first Air Pollution Information Training Center, devoted entirely to air pollution, has been established in New York City?

The Center is one of two being formed by the New York State Action for Clean Air Committee, which is sponsored by the New York State Tuberculosis and Respiratory Disease Association, the Associated Industries of New York State, the Medical Society of the State of New York and the New York State Air Pollution Control Board.

According to its Director, Dr. Leonard Greenburg, former Commissioner of Air Pollution Control of New York City, the Center will fill the need of researchers, engineers, program administrators and the public, and it will serve by fund raising, coordinating research, collecting and transmitting technical information, and training technical personnel and educators. (7)

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EDITORIAL DESK

AVAILABILITY OF PSYCHIATRIC RESIDENCIES IN NAVAL HOSPITALS

The Neuropsychiatric Branch announces the availability of a limited number of vacancies in the approved Navy psychiatric residency training program. Each year there are only twelve openings for Navy psychiatric residents beginning at the first year level. The Navy hospitals which have residency training programs in psychiatry are Bethesda, Maryland; Oakland, California; and Philadelphia, Pennsylvania. Currently, Bethesda and Oakland are fully approved for the required three years' training. Philadelphia is approved for two years' training (the third year being given at Bethesda); plans are underway for obtaining approval for third-year training at Philadelphia to bring the program there up to full accreditation.

Prospective residents often ask whether any Naval hospital can offer completely satisfactory residency training utilizing its own facilities and at the same time meet the requirements of the review committees of the various national approving and accrediting bodies. The same question could be asked of any hospital, civilian or military. The Navy's psychiatric residency training program, as necessary, affiliates with local civilian psychiatric facilities in rounding out certain aspects of the training program. Affiliation with state psychiatric hospitals affords extensive experience with chronic hospitalized psychotic patients. Full time assignments may also be made in one or more of the three programs for the purpose of acquiring experience in neurology, in psychiatric outpatient clinics and in child guidance clinics. Civilian consultants also participate extensively in the program by conducting regular seminars and supervising long term therapy cases. The training experience in Navy hospitals includes inpatient and outpatient psychiatry ranging through the entire diagnostic spectrum. Types of therapy taught and utilized include all that are available, i.e., individual and group psychotherapy, chemotherapy, somatic therapy, occupational, and milieu therapies. Both male and female patients of all ages are seen for evaluation and treatment as indicated. Each training hospital is located in a metropolitan area where there are available academic lectures, short courses, and medical schools with excellent psychiatric departments. The psychiatric training program is further enhanced by relevant research programs of considerable variety. Thus, it can be seen, the resident is exposed to and guided through an extensive range of clinical and academic psychiatry.

Upon completion of residency training, psychiatrists have available a wide variety of assignments offering diverse opportunities and challenges, ranging from assignment to the staff of neuropsychiatric training hospitals to duty as psychiatrist with a Marine Division. Each of the assignments includes ongoing professional experience as well as increasing responsibilities commensurate with the individual's training, experience and motivation. Tours of duty are relatively stable, depending upon the individual situation and needs of the service. The career Navy psychiatrist can expect to progress to Board certification, again depending upon his own motivation,

and to increasingly responsible assignments up to Chief of the Neuropsychiatric Service of a residency training hospital.

The Surgeon General's Consultant Panel in Neuropsychiatry includes the following members who are prominent in their fields. Members of the Panel provide ready sources of assistance and guidance in dealing with all aspects of Navy neuropsychiatry.

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Applications are reviewed by the Surgeon General's Advisory Board which selects residents for training. Although most residencies start in July of each year, for some years residents have been started in psychiatry at other times of the year varying with vacancies available at individual hospitals which result from completion of residency training by other individuals. Inquiry for further details can be made directly to this office. We invite those interested to write to:

Neuropsychiatry Branch (Code 313)
Bureau of Medicine and Surgery
Navy Department
Washington, D.C. 20390

NOT JUST ANOTHER BABY

Mark David Lyons, son of David Lyons HN and Mrs. Lyons was born on July 4th. Two and a half months later in September he was discharged from our hospital.

There are many babies born at USNH Jacksonville; however, this is not just another baby. Little Mark was delivered by Dr. Blair three months prematurely and weighed 1 pound 11 oz. His weight declined the first few days and, at one point, he weighed 1 pound 5 oz.

He spent two months in an incubator and was fed for the first three weeks through a levin tube before changing to a bottle. Under the watchful eye of Drs. Cilento, and Williams and the nursery staff, Mark started to gradually gain weight. Recently, he was taken out of the incubator and, at the time of his discharge, he weighed 5 pounds ¼ oz.

Infants born in this weight range seldom survive due to generalized inability of all their organ-systems to function, particularly the lungs. Moreover, they are deprived of needed nutritional stores and are virtually devoid of all antibodies to fight infection. Amazingly enough, infant Mark never experienced any respiratory difficulty. His uncomplicated story in the nursery is the envy of all preemies.

September 20th was a happy day in the life of the Lyons family. After more than two and one half months, Carol and Dave will be able to hold the "little fella" (to use one of Dave's sayings) and take over the duties of a mother and father.

Pictured above (l to r) are CAPT F. W. Burke MC, Chief of OB-GYN; Dr. Erbs, Dave, Carol, Dr. Williams, Miss Nelson and Dr. Cilento. This is the staff that took care of Mark during his stay in the hospital. Miss Nelson is Head Nurse of the E-Building.—Service Information Officer, U.S. Naval Hospital, Jacksonville, Florida.

ETHER PEROXIDES

A recent occurrence at Chico State College emphasizes the need for special procedures and precautions in the handling and storage of ether compounds. An assistant professor of chemistry at the college, making a routine check of the contents of a storeroom, noticed a partially full five gallon can of isopropyl ether and recalled reading recently about potentially dangerous properties of certain ethers. The article he remembered had stressed the property of many ether compounds to form peroxides under certain conditions of storage or use, and that these peroxides were potentially very powerful explosives which could be initiated by heat or shock.

The authorities were alerted and a special army detonation squad was called in to assist in disposal of the suspect container. After appropriate precaution, the container was removed to an isolated location and exploded with a detonating substance. The resulting explosion, far greater than could be attributed to the initiating charge itself, was violent enough to rattle windows almost a mile away and was heard over three miles away.

Other recently reported incidents illustrate the potential hazard of ether peroxides. At the University of Maine, two glass bottles of slightly less than one gallon capacity, labeled isopropyl ether, were found in a basement storeroom and apparently had been there for more than twenty years. Both bottles were nearly one-third full of a crystalline solid under the liquid upper layer. Aware of the peroxide hazard, the school authorities removed the bottles to a dump at the edge of town and then threw stones at the bottles to break them. The report goes on to state, "When the first stone struck, there was a violent explosion which blasted mud and debris over the surrounding landscape."

Unfortunately, not all the incidents have had happy endings. A chemist was attempting to loosen the stuck glass cap on a pint bottle of isopropyl ether and just as the cap broke loose the bottle exploded violently and the man died from the injuries received.

There are a great many different ether compounds, all being grouped in the same chemical "family" because of similarity in chemical structure and behavior. Other common families are the alcohols, acids, esters, etc. The best known and most commonly used ether is ethyl ether, also known as diethyl ether and sometimes as "sulfuric" ether. This compound finds frequent use as an industrial and laboratory solvent, and also is the ether most commonly used as an anesthetic. Another anesthetic ether is divinyl ether. Isopropyl ether has been advocated as a safer variety for many laboratory uses, because it is considerably less volatile than ethyl ether. Anhydrous or absolute ether is ethyl ether with all traces of impurities and water removed, making it chemically pure. There are many, many other ether compounds but these are the most common ones.

At the present time, little is known about the mechanism which causes the spontaneous formation of peroxides in various ethers, nor is the exact chemical nature of these peroxides known. There appears to be ample evidence however that all the ethers mentioned above are subject to this hazardous property.

Experience has indicated that while the formation of peroxides can occur under any condition, the reaction apparently is accelerated by exposure to light, and oxygen from the air. Contact with certain metals, particularly iron and copper, appears to inhibit peroxide formation but there is no evidence available yet to prove that the formation of peroxides can be entirely prevented.

The following facts regarding formation of peroxides seem to be established:

1. Exposure to the air, as in opened and partially emptied containers, accelerates formation of peroxides.

2. Exposure to light, as would occur in the case of storage in clear glass bottles, encourages formation.

3. Absolute ether undergoes oxidation (formation of peroxides) much more readily than ethyl ether containing a few tenths of a per cent of water.

4. Isopropyl ether may be more vulnerable than other commonly used ethers to peroxide formation on long storage.

5. Heat encourages the inception of oxidation.

6. Distillation of ether containing peroxides greatly aggravates the potential hazard since the portion remaining in the heated distilling flask becomes more and more concentrated as the operation proceeds, in addition to the possibility of accelerated oxidation due to heat.

7. Some but not necessarily all ether peroxides are crystalline solids which would be plainly visible at the bottom of a container. Also, some are water soluble and others are not.

The following general preventive measures are recommended for minimizing the hazards of peroxide formation in ethers:

1. Glass containers of all sizes should be avoided whenever possible.

2. All containers should be dated so that the age of the contents may be determined.

3. Isopropyl and absolute ethers should not be kept for more than six months, ethyl and other ethers for not more than one year.

4. Ether should be stored in as cool a location as feasible, (but not stored in refrigerators unless explosion-proof).

5. Ether should always be tested for peroxide content before any distillation procedure, and of course should not be used if peroxides are found to be present.

6. Do not attempt to open any containers of uncertain age or condition, or whose cap or stopper is tightly stuck.

7. Manufacturers should be contacted to learn any general recommendations regarding safe handling in storage and use, and any specific recommendations for the addition of inhibitors to prevent peroxide formation wherever possible. Manufacturers can also recommend regarding the best methods for chemical test to detect peroxide content, and for possible removal of peroxides by chemical means.

8. In addition to all the above, special precautions are appropriate to hospital use of ether for anesthesia. Section A 1113, Appendix A of N.B.F.U. No. 56, Standard for the Use of Flammable Anesthetics, states as follows:

"The Committee on Hospitals is cognizant of suggestions that the detonation of ether peroxides formed by the oxidation of ether over a period of time may be cause of explosions in anesthesia machines. This has not as yet been experimentally verified, but until further information is secured, frequent emptying of the ether bottle and cleaning of the ether evaporator inside anesthetizing locations would be a simple and desirable precaution."

Finally, if suspect containers are found in storage, do not undertake their removal and disposition on your own! Call the local fire authority. While there appears to be no evidence that peroxides in storage containers have exploded spontaneously, or even under gentle handling, there can be no assurance that this might not occur. Let the local fire authority determine the safest procedure for disposition of the material.—State of California, Public Safety Agency.

REPLACEMENT OF BLOOD USED BY FAMILY MEMBERS OF OVERSEAS SERVICEMEN

The following information has been received from the American National Red Cross:

"In conformity with our continuing policy of being of service to military personnel overseas and in recognition of the active support of the American Red Cross Blood Program by military personnel, any request made through Red Cross by a serviceman overseas for blood replacement for immediate family members hospitalized in the United States will be accepted for the total amount of blood actually transfused (contingent only upon the hospital's acceptance of Red Cross blood or blood credits). Such requests will be assigned by national headquarters to a Red Cross blood center, usually the nearest to the hospital or the one which may have received blood donations from the serviceman's stateside station. Donation of blood overseas is neither a prerequisite nor a requirement."

REIMBURSING COSTS UNDER THE MEDICARE PROGRAM

Representatives of the insurance industry met during the 3rd week in October at Social Security headquarters in Baltimore to discuss the principles to be followed in reimbursing administrative agents for their costs in receiving and paying hospital and medical bills under the medicare program.

Under the law the Government will not make direct payments to physicians, hospitals, and institutions which provide care to persons 65 and over unless the provider of services elects to be paid directly.

Hospitals, nursing homes, and home health care agencies may nominate administrative agents to act as fiscal intermediaries between them and the Federal Government in determining payments due and in paying the bills.

The Secretary of Health, Education, and Welfare, will select "carriers" to determine what are reasonable charges for the reimbursement of physicians and providers of medical services outside the hospital and will pay those bills.

Under agreements or contracts entered with the Secretary of Health, Education, and Welfare, administrative agents will receive advances of funds for the purpose of making benefit payments and as a working fund to cover administrative expenses.

"The Government will be placing great reliance on the responsibility, the efficiency, and the experience of private insurance organizations," Robert M.

Ball, Commissioner of Social Security, told the group meeting this week. "The effectiveness with which they carry out their functions as agents under the program will govern the effectiveness of the program itself," he said.

The consultant group is one of nine work groups that are being called upon to contribute experience and advice to help the Social Security Administration develop policies for the administration of the new program of health insurance for the aged.

Results of the discussions at this week's meeting will be presented to the Health Insurance Benefits Advisory Council, a permanent 16-member council to be appointed in accordance with the law by the Secretary of Health, Education, and Welfare. The Advisory Council will advise the Government on administrative policies and on the formulation of regulations for the medicare program.—USDHEW, Social Security Administration.

PRINCIPLES FOR REIMBURSING HOSPITALS UNDER THE MEDICARE PROGRAM

Principles for reimbursing hospitals under the new medicare program were discussed by an advisory group of 31 consultants, meeting October 11 and 12, at social security headquarters in Baltimore.

The results of the discussions will be used to develop regulations for the payment of hospital costs for the 19 million people 65 and over who will be covered by the program of hospital insurance for the aged when it goes into operation next July.

The law specifies that hospitals shall be reimbursed for the reasonable cost of care provided the aged. They will be paid for their actual costs, determined under a national formula which will be designed to take account of differences in cost from hospital to hospital, reflecting such factors as differences in the quality and intensity of care they provide.

"By meeting the full reasonable cost of care, the law will provide financial support for the best quality of care that hospitals can provide," Robert M. Ball, Commissioner of Social Security, told the group.

The advisory group, composed of representatives of the medical profession, hospitals, health insurance organizations, and others involved in the provision of health services, is one of nine work groups that will be called upon to contribute experience and advice to help the Social Security Administration develop policies for the administration of the new programs hospital insurance and medical insurance set up in the medicare legislation.

"Hospitals will no longer have to struggle as they have with the inability of older people to pay for their hospital care," Ball said. "Their losses from bad debts and from providing care free to aged patients will be reduced and will not have to be included in charges to paying patients."—USDHEW, Social Security Administration.

NAVY CORPSMAN CITED FOR BRAVERY

Hospitalman George M. Aurelius became the second Navy Corpsman to be decorated with the Bronze Star Medal with Combat "V" recently when the award was presented by Maj. Gen. Lewis W. Walt, Commanding General of the 3rd Marine Amphibious Force.

Aurelius received his award while serving with D Co., 3rd Reconnaissance Bn.

Hospitalman George M. Aurelius is congratulated by Maj. Gen. Lewis W. Walt, Commanding General of the 3rd Marine Amphibious Force, after being presented the Bronze Star with Combat "V". He was cited for administering aid to two marines wounded on a mission north of the DaNang airfield.

On July 12, Aurelius was accompanying a search-and-clear mission of a village north of the DaNang airfield when the patrol received heavy small arms fire from the Viet Cong.

The platoon was pinned down by fire and sustained two casualties. Aurelius quickly and competently administered aid to the injured men, exposing himself to enemy fire.

He hurt his knee while rushing to the wounded marines but refused evacuation for himself, knowing he was the only corpsman attached to the company. —Technical Information Office, BuMed.

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